

ECOG Phase I and II Monitoring Policy

Introduction

ECOG is a cooperative group funded by the Cancer Therapy Evaluation Program (CTEP) of NCI, and operates in accordance with CTEP requirements. All phase I and II studies coordinated by ECOG are monitored using the procedures outlined in this document.

Adverse Events

All ECOG protocols contain a section describing procedures for expedited reporting of classes of adverse events (AEs). These procedures are reviewed and approved by CTEP prior to protocol activation. Participating institutions are required to follow protocol requirements for submission of expedited reports of adverse events. As of January 1, 2001, ECOG is following the requirements of CTEP's AdEERS system for expedited adverse event reporting on all studies that use investigational agents supplied by CTEP. For all studies, ECOG ensures that NCI, industry sponsors, and the FDA receive reports as appropriate. For studies requiring it, ECOG reports adverse events to CTEP for forwarding to the NIH Office of Biotechnology Activities.

Cumulative summaries of expedited adverse event reports are automatically generated every month for all ECOG studies. Those studies with at least 1 death on treatment in the previous month, 2 events in the previous month or 6 events in the previous 6 months are reviewed by Coordinating Center staff, the study statistician, the study chair, and a disease-specific toxicity monitor. If any of the reviewers feel that further review is necessary, the reports are distributed and then discussed on a conference call. If the reviewers feel it necessary, the protocol can then be amended or suspended. In the event of a very serious situation, the Group Chair can suspend the study prior to the detailed review.

All toxicities, regardless of whether expedited reporting is required, must be reported to the ECOG Coordinating Center as part of routine data submission. The Data Associates monitor these data to ensure that all required AEs have had expedited reports submitted. Summary analyses of the toxicity data are performed twice each year. These summaries are distributed to the local investigators, who are responsible for providing them to their local IRBs.

Safety Reports from Industry or the NCI are forwarded immediately to investigators. Protocol amendments are written when required (e.g., amendments in the consent form).

Outcome Data

Outcome data are monitored by the ECOG Coordinating Center staff, the study statistician, and the study chair. If the study has a two-stage accrual design, then accrual will be suspended following completion of the first stage of accrual unless sufficient information is already available to determine whether the criteria for proceeding to the second stage have been met. The determination of whether the protocol criteria for proceeding to the second stage have been met will be made by ECOG Coordinating Center staff, the study statistician, and the study chair.

Data Integrity/Completeness

ECOG has extensive quality control procedures for trial data. All data are reviewed by trained Data Associates in the Coordinating Center and by the study chair for the trial. Data clarification forms (DCF) are sent to the institutions for clarification/missing data. ECOG also has an on-site audit program for source verification of data. This program complies with CTEP policy.

Accrual Rates

The Group Chair and Group Statistician monitor the progress of phase I and II trials in conjunction with the study chair, study statistician, and disease committee chair. If accrual is slower than expected, modifications to trial design may be considered or the study may be closed.

Retention of Participants/Adherence to Protocol

ECOG monitors “lost to follow-up” rates at participating sites as part of its institution performance monitoring process. Protocol compliance is also monitored. Institutions who fail to meet Group standards can be suspended/dropped from Group membership.

Additional Procedures

In addition to the procedures stated above, ECOG has the following procedures to monitor phase I studies:

- Only a limited number of institutions (usually 2 to 6) are allowed to participate in ECOG phase I studies. Each institution must fax or express mail study data to the study chair and Coordinating Center weekly while the patient is on treatment. Institutions are required to telephone the Coordinating Center, NCI, and study chair within 24 hours of any death, the first occurrence of a previously unknown clinical event, and all life-threatening (grade 4) toxicities. The study chair will notify the other participants of the study through the ECOG electronic mail system of any potential dose-limiting toxicity or telephoned adverse events. An e-mail user group is set up for each phase I study to include the study chair, co-chair, all participating investigators and designated nurses/CRAs, study statistician, and phase I personnel at the ECOG Coordinating Center.

- Dose escalations are usually discussed on conference calls with, at minimum, the study chair, co-chair, ECOG Data Associate, and the study statistician, although a call is not required if all parties agree that escalation is appropriate. Institutions are notified of accrual suspensions via ECOG electronic mail after each dose level is filled. Overaccrual to any dose level is not allowed, and this is enforced by the ECOG registration system.
- For phase I studies monitored by Theradex, a CTEP contractor, data are forwarded from ECOG to Theradex, and the data processing is done by Theradex. The administrative management of the study is as described above.

1. Document Revision History

| Version | Summary of Revisions | Approved | Implemented |
|---------|---|---------------|---------------|
| v1 | Original Web site version | 2008 | 2008 |
| v2 | Updates to job titles, change of document template, minor terminology corrections | July 12, 2009 | July 12, 2009 |
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2. Document Reviewers

| Reviewer Name | Reviewer Name |
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