Development and Implications of a Redacted Clinical Trial Protocol for Posting Online With the Published Manuscripts

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Background

- Increasingly, journals are requiring submission of clinical trial protocols for phase II and III studies which can be redacted to protect proprietary information.
  - Rationale: Access to the study protocol assists the editors and reviewers in properly peer reviewing the manuscript.
    - Online posting of the protocol will allow readers to properly interpret an article.
- This trend is in line with ensuring unbiased review and transparency of scientific publications and sponsor's obligation to register clinical trials.

Clinical Protocol Request from Leading Medical Journals

- ***New England Journal of Medicine*** (March 2, 2011)
  - Requested a copy of the clinical protocol to post with the online publication.
  - Asked to redact proprietary information from the protocol before submission.
- ***Lancet*** (March 22, 2011)
  - Requested authors to post the clinical protocol on a publicly accessible website.
  - Stated that a link to the website will be put in the publication.

Clinical Protocol Request from Leading Medical Journals (contd)

http://jco.ascopubs.org/site/ifc/protocol.xhtml

- ***Journal of Clinical Oncology:*** *JCO* believes that for the editors and reviewers to properly peer review a submission, as well as for readers to thoroughly interpret an article, a redaction of the protocol for all randomized phase II and III studies must be provided.
  - It is the responsibility of the authors to submit; do not submit the full protocol.
  - It will be available to the editors and reviewers during the peer review process and, if your manuscript is accepted, will be published online.

Clinical Protocol: Table of Contents

Typical Phase III Protocol >100 pages

TABLE OF CONTENTS

Redacted Protocol Content

Guidelines: *Journal of Clinical Oncology*

http://jco.ascopubs.org/site/ifc/protocol.xhtml

- Selection of patients, including both eligibility and ineligibility criteria.
- Schema and treatment plan, including administration schedule.
- Rules for dose modification.
- Measurement of treatment effect including response criteria, definitions of response and survival, and methods of measurement.
- Reasons for early cessation of trial therapy.
- Objectives and entire statistical methods section (including end points).

Protocol Elements for Redacted Protocol Template

Journal of Clinical Oncology

Objectives (2)

Schema and treatment plan, including administration schedule (3)

Selection of patients, including both eligibility and ineligibility criteria (4)

Rules for dose modification (6)

Measurement of treatment effect including response criteria, definitions of response and survival, and methods of measurement (9)

Reasons for early cessation of trial therapy (10)

Entire statistical methods section (including end points) (11)

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Redacted Protocol Template: Table of Contents

TABLE OF CONTENTS

Considerations for Creating Redacted Protocol

- Use most current version of protocol.
- Redact all proprietary information.
- Provide the requested information from the guidelines.
- Limit text to protocol-specified efficacy and safety evaluations.
- Use tabular format where possible. For example, the ‘Time and Events Schedules’ can be used to summarize the frequency and timing of the pharmacokinetic, efficacy, safety, and other measurements.
- Redact all ‘exploratory’ analysis proposed in the original protocol (may impact future IP issues).

Creating Redacted Protocol for Journal use

TABLE OF CONTENTS

INVESTIGATOR AGREEMENT
LIST OF ATTACHMENTS
LIST OF IN-TEXT TABLES AND FIGURES
SYNOPSIS
TIME AND EVENTS SCHEDULE
ABBREVIATIONS

1. INTRODUCTION
2. **OBJECTIVE AND HYPOTHESIS**
3. **STUDY DESIGN AND RATIONALE**
4. **SUBJECT SELECTION**
5. TREATMENT ALLOCATION AND BLINDING
6. **DOSAGE AND ADMINISTRATION**
7. TREATMENT COMPLIANCE
8. CONCOMITANT THERAPY
9. **STUDY EVALUATIONS**
10. **SUBJECT COMPLETION/WITHDRAWAL**
11. **STATISTICAL METHODS**
12. ADVERSE EVENT REPORTING
13. PRODUCT QUALITY COMPLAINT HANDLING
14. STUDY DRUG INFORMATION
15. STUDY-SPECIFIC MATERIALS
16. ETHICAL ASPECTS
17. ADMINISTRATIVE REQUIREMENTS

Phase III Protocol
Total length = 143 pages

TABLE OF CONTENTS

ABBREVIATIONS

1. OBJECTIVES
2. TREATMENT PLAN
3. SUBJECT SELECTION
4. DOSAGE AND ADMINISTRATION
5. TREATMENT EFFECT
6. DISCONTINUATION OF TREATMENT
7. STATISTICAL METHODS

Redacted Protocol
Total length = 16 pages

Implications for Redacted Protocol

- Will all journals require redacted protocols analogous to registration of clinical trials?
- What if individual journals have their own requirements for content?
- Where should the redacted protocol be stored so it is 1) not mistaken for the original protocol and 2) can be used by multiple teams for multiple publication submissions?
- How to handle protocol amendments?
- Review/approval process for redacted protocols.
- Concerns for intellectual property.
- Resource implications.

Summary

- Leading medical journals are requesting redacted versions of Phase II and Phase III clinical study protocols.
- We created a redacted protocol template based on guidelines provided by The *Journal of Clinical Oncology.*
- Several considerations:
  - Use the latest version of protocol.
  - Provide protocol-specified efficacy and safety.
  - Redact all proprietary information.
  - Redact all exploratory analysis information.

Transitional Slide

(between presentations within a segment)