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

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DISCLOSURE

• Namit Ghildyal: Employee of Janssen Research & Development, LLC, Raritan, NJ, USA. Holds stock in Johnson & Johnson

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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**

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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**
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

**Objective**

- 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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*Journal of Clinical Oncology*
Redacted Protocol Template: Table of Contents

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5. → TREATMENT EFFECT ........................................................................................... 2

6. → DISCONTINUATION OF TREATMENT ................................................................... 2

7. → STATISTICAL METHODS ...................................................................................... 3
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

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Phase III Protocol
Total length = 143 pages

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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)