Patient Case Records Review

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Alliance for Clinical Trials in Oncology

Audit Workshop - Alliance Group Meeting – November 2, 2017
6 Categories

- Informed Consent
- Eligibility
- Treatment
- Disease Outcome/Response
- Adverse Events/Study Parameters
- General Data Quality
Informed Consent
Informed Consent

- Participant signed, dated prior to undergoing any study related procedures
- All required signatures are present
- Current, IRB-approved CF was used
- Documentation of the informed consent process exists
- Any required re-consents
- Non English speaking subjects
Eligibility
Eligibility

- Documentation that all eligibility criteria have been met as specified by the protocol
- All required tests to confirm eligibility were performed prior to registration
- Tests done within protocol time limits
Treatment

Cancer treatment

Diagnosis accuracy and diversity of modern treatment methods allow to choose the most effective set of treatment for each patient individually. Local treatment is not toxic, has no contraindications to repeated use.
Treatment

- Specific protocol treatment was given
- Treatment not given until after registration unless specifically allowed in the protocol
- Treatment given per protocol timeframe (cycle length, within window post-op, etc)
- Dose Deviations/Modifications
- Additional agent/treatment given?
Disease Outcome/Response
Disease Outcome/Response

- Accurate documentation of initial sites of involvement
- Re-evaluation of status performed according to protocol
- Protocol-directed response criteria followed
- Verify claimed response (PR, CR)
Adverse Events
Adverse Events/Study Parameters

- Follow-up studies necessary to assess adverse events (AEs) were performed (study calendar)
- Grades, types, and attribution of AEs are documented in source and are accurately recorded in CRFs
- Adverse Event Expedited Reporting filed for required toxicity (CTEP-AERs)
General Data Quality

- Accurate and consistent
- Healthcare documentation
- Timely and Accessible
- Complete
- Interoperable and Auditable
General Data Quality

- Data accurately reported on CRFs
- Forms complete
- Data submitted in a timely manner
- Concordance with source documentation
- Supplemental reports submitted
- Specimens submitted
Source Documents

**EMR**: must have a local staff person as the “driver”; official back-up for research folders

**Paper records, Research folders:**
- Attributable: is it obvious who wrote it?
- Legible: can it be read?
- Original: is it a copy; has it been altered?

**Imaging**: have access to images available

**Delegation of Tasks Log (DTL)** have copy available
Audit Preparation
Preparing for an Audit

- Attend the Audit Workshop!
- Review Alliance Audit Policies and Procedures
  - Institutional audits: Policy number 2.8
    - Alliance auditors will not complete site-specific training: 2.8.5.5
      - Auditors are current with Human Subjects training
  - Audit preparation by the institution: 2.8.6
  - Conduct of an Alliance audit: 2.8.7
  - Review of patient case records: 2.8.7.4
Preparing for an Audit

- Ensure that arrangements have been made:
  - Reserve conference room
  - Notify appropriate personnel
  - Request all required materials including a paper copy of all protocols
  - Ensure Principal Investigator available for the Exit Interview
- Review your records!
Sometimes we call in expert assistants!
Deficiencies
What is a Critical Deficiency
CTMB Guidelines Section 5.1

- Any condition, practice, process or pattern that adversely affect the rights, safety or well-being of the patient/study participant and/or the quality and integrity of the data; includes serious violation of safeguards in place to ensure safety of a patient/study participant and/or manipulation and intentional misrepresentation of data.
What is a Major Deficiency

- A variance from protocol-specific procedures that makes the resulting data questionable.
- An unacceptable frequency of lesser deficiencies may be treated as a major deficiency.
What is a Lesser Deficiency

- A deficiency that is judged not to have a significant impact on the outcome or interpretation of the study and is not described as a major deficiency.
OK, Lesser, Major or Critical?

- Patient Case Review – 
  Informed Consent

Consent form document was not signed and dated by the study participant (or legally authorized representative, if applicable).
OK, Lesser, Major or Critical?

- Patient Case Review –
  Informed Consent

The consent form that the patient signed had a sentence crossed-out. The applicable IRB approved CF had the sentence included.
OK, Lesser, Major or Critical?

- Patient Case Review – Eligibility

A pregnancy test was not done pre-randomization in this documented pre-menopausal patient. There was no documentation regarding sexual activity and/or use of contraceptives. Of note, a pregnancy test done after randomization but before treatment was negative.
OK, Lesser, Major or Critical?

- Patient Case Review – Eligibility

  The physician signed and dated an eligibility checklist indicating that all eligibility criteria are met. The protocol requires an absolute B cell lymphocyte count $>5000/\mu$L, but the lab result printout indicates the value is 3673/\mu$L.
OK, Lesser, Major or Critical?

- Patient Case Review – Treatment

The protocol treatment includes sunitinib, but due to high cost, the physician prescribed pazopanib.
OK, Lesser, Major or Critical?

- Patient Case Review – Adverse Event/Study Parameters

Required chemistry labs were not checked on day 15 of the treatment cycles.
OK, Lesser, Major or Critical?

- Patient Case Review – Adverse Event/Study Parameters

A CTEP-AERs report (expedited adverse event reporting) was not submitted for cycle 1 hospitalization due to neutropenia.
A041501

Additional Instructions or Exclusion to CTEP-AERS Expedited Reporting Requirements for Phase 2 and 3 Trials Utilizing an Agent Under a non-CTEP IND:

• All adverse events reported via CTEP-AERS (i.e., serious adverse events) should also be forwarded to your local IRB.

• Grade 3/4 hematopsuppression and hospitalization resulting from such do not require CTEP-AERS, but should be submitted via routine AE reporting.

• Grade 1-3 fatigue and hospitalization resulting from such do not require expedited reporting via CTEP-AERS reporting, but should be reported via routine AE reporting.

• Grade 1-2 alopecia and hospitalization resulting from such do not require expedited reporting via CTEP-AERS reporting, but should be reported via routine AE reporting.
OK, Lesser, Major or Critical?

- Patient Case Review – Disease Response/Outcome

Imaging reports were not available for auditors to review. Unable to confirm reported date of progression.
OK, Lesser, Major or Critical?

- Patient Case Review – Disease Response/Outcome

The subject has been non-compliant with follow-up scans and visits. There is good documentation of clinic scheduling and attempts to contact the subject.
OK, Lesser, Major or Critical?

- Patient Case Review – General Data Quality

The on-study form due at baseline (10/19/14) was submitted 3/12/15 (3-6 months late).
OK, Lesser, Major or Critical?

- Patient Case Review – General Data Quality

The reported baseline value of AST is 43, but source documentation indicates value should be 53.
OK, Lesser, Major or Critical?

- Patient Case Review – General Data Quality
  
  The frozen specimens due at baseline were not submitted to the Pathology Coordinating Office by the time of the audit, 2 years later.
Common Findings
Common Findings

- **Informed Consent**
  - Re-consenting not done
  - Blanks remain blank

- **Eligibility**
  - Performance status not documented
  - Tests done out of window

- **Treatment**
  - Oral compliance not documented
  - Dose modifications not done or not within requirements of the protocol
Common Findings

- **Disease Outcome/Response**
  - All initial sites of disease not reported at baseline
  - Imaging, physical exams etc not done per schedule

- **Adverse Events/Study Parameters**
  - Toxicity assessments not performed or inconsistent
  - Unnecessary reporting of AEs < grade 3
## Adverse Events: Solicited

<table>
<thead>
<tr>
<th>Adverse event term (v4.0)</th>
<th>MedDRA AE code (CTCAE v4.0)</th>
<th>Adverse event not evaluated</th>
<th>Adverse event grade (highest grade this reporting period)</th>
<th>AE attribution (if grade &gt;0)</th>
<th>Has an adverse event expedited report been submitted?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tinnitus</td>
<td>10043882</td>
<td>☐</td>
<td>0 1 2 3</td>
<td>□ Unrelated</td>
<td>□ Yes □ No</td>
</tr>
</tbody>
</table>

Were *(other)* adverse events assessed during this reporting period? *(check one)*
- ☐ Yes, and reportable adverse events occurred *(go to Adverse Events: Other CRF)*
- ☐ Yes, but no reportable adverse events occurred
- ☐ No
Adverse Events: Other

**INSTRUCTIONS:** Record all adverse events beyond those solicited; record grade 1 & 2 with attribution of possible, probable or definite and all grade 3, 4 and 5 regardless of attribution. (Both hematologic and non-hematologic adverse events must be graded on this form as applicable.)

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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>INCLUDE GRADE 0’s</td>
<td>□ Unrelated</td>
<td>□ Yes □ No</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0 1 2 3 4 5 (death)</td>
<td>□ Unlikely</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>□ Possible</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>□ Probable</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>□ Definite</td>
<td></td>
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</tbody>
</table>

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Common Findings

- General Data Quality
  - Form instructions not followed
  - Delinquent data
  - Supplemental reports not submitted
  - Specimens not collected/submitted
Component Evaluation
CTMB Guidelines Section 5.4.2

- Acceptable
  - No Major deficiencies found during the audit
  - Acceptable needs follow-up
    - One or more Major deficiencies or multiple Lesser deficiencies found
- Unacceptable
  - Multiple Major deficiencies or a single critical deficiency found (re-audit required)
Want an easier audit day?

- Document!
  - If it is not documented, it did not happen
- Communicate!
  - Don’t be afraid to ask questions to your staff and/or the audit team
- Keep records audit ready!
  - Tag paper charts or keep summary sheet for electronic records as you go along
Summary Sheet

Alliance Study #  Patient #

Signed ICF:
Enrolled:

Eligibility
Path:
H&P:
Labs:
CT chest & up abd:
Bone Scan:
Other:

Treatment
Cycle 1
Cycle 2
Cycle 3
Cycle 4
Cycle 5
Cycle 6

Response
Prior to Cycle 3 scan
Prior to Cycle 5 scan
End of treatment
Relapse

Last Follow-up
Resources

The Alliance for Clinical Trials in Oncology
www.allianceforclinicaltrialsinoncology.org

FDA Code of Federal Regulations
https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm

Cancer Therapy Evaluation Program (CTEP)
CTMB Audit Guidelines
Questions?
2017 Fall Group Meeting

November 2 – 4 / Chicago, IL