Patient Case Records Review

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Audit Workshop - Alliance Group Meeting – November 1, 2018
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
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

Pain

- Swelling
- Back pain
- Hair loss
- Light-headed
- Blurry
- Insomnia
- Dizziness
- Worried
- Help
- Bright spots

Painful

- Can’t sleep
- Dull
- Neck ache
- Sore
- Crying
- Weird spots
- Pounding heart

Emotional

- Feel funny
- Tired
- Depressed
- Angry
- Terrified
- Spasm

Other

- Uncomfortable
- Weak
- Help
- Bright spots
- Nausea
- Rash
- Punctured ear
- Rash
- Uncomfortable
- Uncomfortable
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
- Complete
- Timely and Accessible
- 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

- **Accurate**: Is the document accurate?

- **Identifiable**: Is the document identifiable?

- **Legible**: Is the document legible?

- **Secure**: Is the document secure?
Source Documents

**EMR:** must comply with 21 CRF part 11 subpart B; must have a local staff person as the “driver”; official back-up for research folders

**Paper records, Research folders:**
- please appropriately tag

**Imaging:** have access to images available when needed for assessing disease response

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

- Attend the Audit Workshop!
- Review Alliance Audit Policies and Procedures
  - Institutional audits: Policy number 2.8
    - 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

- **Alliance auditors will not complete site-specific training: 2.8.5.7**
  - **Auditors:**
    - are current with Human Subjects training
    - have a signed Alliance Confidentiality agreement on file
    - have completed mandatory CTMB auditor training
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

The patient was enrolled into the study on 5/11/18. The consent form is dated 7/24/18.
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 a hemoglobin of ≥ 12.0 g/dl, but the lab result printout indicates the value is 11.8 g/dl.
OK, Lesser, Major or Critical?

- Patient Case Review – Treatment

The protocol treatment was not dose reduced per protocol guidelines. Blinotumumab 28 mcg/d was given for 8 days rather than 9 mcg/d.
OK, Lesser, Major or Critical?

- Patient Case Review – Treatment

Internal mammary lymph nodes were not included in the radiation field, as required by the protocol.
OK, Lesser, Major or Critical?

- Patient Case Review –
  Adverse Event/Study Parameters

Required labs were not done according to the study calendar.
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.
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 hematosuppression 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

The baseline tumor measurement form did not include a liver lesion that was 2 x 4 cm.
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 research blood specimens due at disease progression were not collected.
Common Findings
Common Findings

- Informed Consent
  - Re-consenting not done
  - Use of out of date consent form
- 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
  ● Lack of concordance between imaging report and RECIST flowsheet

● 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</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>INCLUDE GRADE 0’s</td>
<td>☐Unlikely</td>
<td>☐No</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>☐Possible</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>☐Probable</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>☐Definite</td>
<td></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.)

<table>
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<tr>
<th>Adverse event term (v4.0)</th>
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<th>Adverse event grade (highest grade this reporting period) INCLUDE GRADE 0's</th>
<th>AE attribution (if grade &gt;0)</th>
<th>Has an adverse event expedited report been submitted?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>0 1 2 3 4 5 (death)</td>
<td>☐ Unrelated</td>
<td>☐ Yes ☐ No</td>
</tr>
</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
    - audit@alliancenctn.org

- **Keep records audit ready!**
  - Tag paper charts or keep summary sheet for electronic records as you go along
## Summary Sheet

### Alliance Study #

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?
2018 Fall Group Meeting

November 1-3/ Chicago, IL