CASE REPORT FORM CORRECTION NOTES

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<th>Pat. No./Initials:</th>
<th>Protocol:</th>
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<td>Investigator:</td>
<td>Monitor:</td>
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<tr>
<th>CRF Page No. / Identifier</th>
<th>CRA’s Comments</th>
<th>Study Staff</th>
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January 7, 1994

Ms.
4141 North Boyle Avenue
Los Angeles, CA 90033

RE:

Dear Ms. :  

I would like to confirm our agenda for the upcoming monitoring visit. As we discussed, the visit is scheduled for January 31st - February 2nd, 1994. I will arrive at the site at approximately 1:30 p.m. on Monday afternoon. I would like to accomplish the following during the visit:

- Complete data clarification queries left at the site during the last monitoring visit.
- Complete and retrieve the data clarification queries mailed to the site after the last monitoring visit.
- Perform Drug Accountability and ship unused study material back to .
- Review completed case report forms (CRFs), source documentation and signed informed consent forms for patients that have been enrolled. Complete corrections from this review.
- Retrieve all completed, reviewed, and corrected CRFs.
- Review Investigator Notebook for completeness.

Please feel free to call me if you have any problems with regard to this proposed schedule. Thank you in advance for your cooperation. I look forward to meeting you.

Sincerely,

Clinical Research Associate

CC:
MONITORING REPORT

Sponsor Name: 
Study Material: 
Protocol #: 
Investigator / Location: 
.M.D. 
1211 Union Avenue 
Memphis, TN 38104 
Visit Date(s): January 27, 1994 
Prev. Visit Date(s): December 16, 1994 
Contacts: M.D. 

Visit Checklist

Within the context of what is acceptable for this project, enter Y (acceptable), N (not acceptable), NA (not applicable), or NE (not evaluated). Comment on any N or NE entries.

Protocol: 
Y Eligibility Criteria Met 
Y Study Evaluations and Procedures Followed 
Y Concomitant Therapy Appropriate 
Y Study Material Administered per Protocol 
NA Serious Adverse Events Reported 
NA Safety Summary Submitted to IRB 

Site Facilities: 
NA Laboratory Facilities Adequate 
NA Study Pharmacy Adequate 
NA Study Facilities Adequate 
NA Study Staff Adequate 
Y Staff Supervised Properly 
Y No Change in Study Staff Since last Visit 
Y Study Supplies Adequate 

Case Report Forms: 
N CRFs Verified Against Source 
Y CRFs Completed Adequately 
Y CRFs Reviewed and Signed by Authorized Staff 
Y CRF Supply Adequate 
N Source Documents Adequate and Available for Review 

Study Material Supplies: 
Y Storage Area Adequate 
Y Study Material Review Performed 
Y Study Material Accountability 
Y Records Accurate
Site Accrual Status

20 Expected  2 Enrolled  0 Number of Screen Failures  
(as defined by project)

0 In Screening  NA Randomized  1 Active  1 Complete

0 Total Patients Discontinued:

Reasons for Discontinuation

Protocol Violation  Treatment Failure  Consent Withdrawn  
Adverse Experience  Lost to Follow-Up  Death  Other (Describe in Comments Section)

Patient Status

Initials/Patient ID #: MRM/001
Informed Consent Date(s): 01/18/94
Visits Monitored: All
Visits Retrieved: None
Protocol Deviations: Yes
Serious/Unexpected Events: No
Comments: The site did not perform the T2 post injection fast spin echo scan. The patient became impatient and did not want to stay for the entire procedure. No case report forms were retrieved due to lack of sufficient source documentation and high probability that additional follow up information may be obtained from this patient. This patient is a candidate for either a lobectomy or a liver transplant and will have one of these procedures done within the next couple of weeks. Dr. indicated that he is aware that it is important to follow this patient through his surgery and to obtain copies of the pathology reports.

Comments

Protocol: The protocol was adhered to with the exception of not completing the post inject T2 fast spin echo as noted above. Dr. indicated that the study manual and protocol that
had sent him was misplaced within the hospital system. The second protocol and study manual was not received until the day after he enrolled patient 001. Dr. stated that because he did not have access to the current protocol, Dr. was unsure which scans to perform, therefore he decided to do all possible scans. The patient refused to stay for the last scan, which would have been the correct scan as per protocol.

discussed with Dr. that serious adverse events that occur within seven days after the injection need to be documented and reported to as soon as the adverse experience is discovered.

Regulatory: reviewed the Regulatory Notebook and noted that the site did not have a signed Form FDA 1572. Dr. indicated that he is unable to locate the signed FDA Form 1572. informed Dr. that she will request from that copy of the list. Mr. will ask his IRB to send him a current membership list.

Site Facilities: The site facilities remain adequate for this study.

Case Report Forms: The case report forms (CRFs) were completed adequately with only a few minor corrections. The following issues were reviewed with Dr. :

- “NA” should be recorded on the Onsite Review (Part 2) for the level of confidence of the lesion diagnosis for each corresponding lesion which has a diagnosis of unknown.

- If the overall hepatic diagnosis for the patient is unknown, then please check the unknown box on the Onsite Review (Part 3) and leave the corresponding boxes pertaining to the level of confidence blank. In all other situations, a level of confidence needs to be recorded for the corresponding lesion diagnosis.

- The Medical History CRF page needs to have the complete date of onset recorded. If the complete date is unknown, then record the portion of the date that is known and record “unk” for the portion of the date that is unknown.

The source documentation was not available for review. The patient’s medical chart is located at Hospital and was inaccessible at the time of this visit. Dr. had photocopied the patient’s process notes and filed them with the CRFs. asked Dr. to also photocopy the patient’s medical history, medication pages and discharge summary. Dr. stated that it would not be a problem obtaining copies of this information and will have all the necessary source documents photocopied by the time of the next monitoring visit.

Dr. stated that he had been using the flow sheets that distributed at the initiation visit. Dr. stated that he was unaware that they were used for source documentation and discarded them after he had completed the CRFs. emphasized to Dr. that the flow
sheets are used as source documents and requested that they be kept with the copies of the patient’s medical notes.

As noted above, within the next couple of weeks additional follow up information will most likely be available for patient 001. Thus, instructed the site to wait to complete the Final Diagnosis CRF pages until the pathology report is available. requested that Dr. keep a copy of the pathology report with the patient’s source documents.

Dr. indicated that the start and stop times recorded for the scans and vital signs were not taken from the same clock. Dr. stated that in the future he will synchronize his watch with the computer clock.

Study Material Supplies:
reviewed the Drug Inventory form and found it to be acceptable.
inventoried the study drug and found two vials have been used and contain remaining study material and eight vials remain unopened.

Summary:
Two patients have been enrolled in the study, one of which has completed the study and one is scheduled to return to the site for the 18-30 hour follow up visit on January 27, 1994. No serious adverse events were reported. The CRFs for patient 001 were reviewed and will be retrieved at the next monitoring visit once Dr. provides sufficient source documentation. The CRFs for patient 002 were not complete, therefore were not reviewed at this visit.

Other:
At the time of this visit, the site had not received the laboratory reports for patient 001. informed Dr. that the reports should be received within 48 hours after specimens are shipped to the site. emphasized to Dr. that it is important that he follow up if he continues to receive laboratory reports late. Dr. stated that he will determine if he has received the laboratory reports today, and if not he will call

Issues for Follow-up:
• Verify that the site has received a copy of the FDA Form 1572.
• Verify that the site has received a copy of patient 001’s pathology report.
• Verify that the site is receiving laboratory report in a timely manner.

Next Monitoring Visit:
The next monitoring visit was tentatively scheduled for Thursday, March 3, 1994.
March 14, 1994

11808 Northup Way, Suite 350
Bellevue, WA 98005

RE:

Dear Ms.

I would like to thank you and for your time spent with me during my March 9th-11th, 1994 monitoring visit.

Summarized below are the issues discovered and addressed during this past visit:

• Case report forms (CRFs) and Informed Consent Forms for patients #S14181 through #S14197 were monitored. Only minor corrections were necessary, and all were completed by either you or .

• The missing Month 13 study medication card for patient LEP/S14185/5112 was reported to and a new card will be sent to you; please notify me when you receive this card;

• Obtain the updated Laboratory manual (dated February 4th, 1994) and file it with the original version in the Regulatory Notebook;

• Any clinically significant event noted on the Chemistry II panel of the laboratory report (this includes the triglycerides and glucose tests) should be treated as any other laboratory adverse event. Please list these events on the Laboratory Adverse Event CRF.

• Please remember to have the patients sign the Patient Visit Sign-In Log for each visit;

• Use generic names for all past hypertensive medications and concomitant medications;

• Please continue to indicate which arm was used to measure blood pressure measurements in the medical chart for each visit;

• Please continue to note in the medical chart the time at which a patient lies down in the examination room for supine blood pressure.

• Please photocopy the Study Drug Administration CRF with the attached drug label for your records;
The list above serves as a friendly reminder of items that we reviewed and discussed. I extend my thanks to you and

for your time and assistance.

As we discussed, my next monitoring visit has been scheduled for April 6th - 7th, 1994 at 10:00 AM. During this visit, I will review patient books for all ongoing and new patients. Kindly have the Informed Consent Forms, CRFs (with completed MDLs), source documents, laboratory results, and drug inventory record available for these patients.

As always, please do not hesitate to contact me at if you have any questions.

Sincerely,

Clinical Research Associate

CC: