
Computerized Adverse Event Reporting (CAER)

Office of Regulatory Affairs
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CAER Raison d'Etre

- Research subject safety and compliance with regulatory requirements
 - Expedited adverse event assessment and reporting
- Facilitation of both internal and external adverse event reporting
 - Most AE reporting systems do not take into consideration the sheer volume of external reports
 - Most institutions are doing sponsored or cooperative group studies, whereby the processing of external reports becomes burdensome.
- Serving IRB's pivotal role in reviewing adverse events
 - Ultimate decisions concerning safety and efficacy are done at the local IRB level
- Central repository of adverse events
 - Cross-trial analyses
 - Search for specific variables
 - Identification of trends
 - "Ad Hoc" and "Preformatted" reporting



CAER Features

- Electronic submission of new and follow-up internal and external adverse event reports
- Creation of amendments
- Algorithmic-like assistance of causal relationship
- Validation of entries for completeness and consistency



CAER Features (Cont'd)

- Trend and root cause analyses
- Email notifications
- Browser and operating system independency
- Cross-referencing among protocols
- Compliance with standards
 - MedDRA
 - Section 508
 - *HL7 messaging Compliant*



Georgetown CAER

Computerized Adverse Event Reporting R3.1

Data Entry Module

Internal AE Reports

External Unexpected AE Reports (use this form if the event is NOT listed in the Informed Consent Form)

External Expected AE Reports (use this form if the event IS listed in the Informed Consent Form)

Enter a protocol

Reporting Module

Search reports

Canned Reports

Administration

Find a report

Ticket:

Find Report

**Georgetown CAER
Summary**

This report was begun on 09/21/2004 at 2:46 PM by Janice Fowler.

- [Amend the report](#)
- [View Summary of IRB Number: 2003-288](#)

Report Summary for Ticket Number 10001830

Event Date: 09/21/2004

Event Ticket: 10001830

IRB Number *Investigator*
2003-288,
Franklin Square
HC
Dr. William Waterfield

Patient: - no patient -

Event Date: 09/21/2004

Report Entered On: 09/21/2004 2:09

Type of SAE Report: External

Final Report Date: 09/21/2004

Reported By: *Janice Fowler*

Event:

PT COMMENCED STUDY THERAPY 16MAR2004, ON 06JUN2004 PT EXPERIENCED SEVERE HYPONATREMIA (SODIUM 116 mmol/l) WITH 'MENTAL ALTERATION', STUDY MEDICATION WAS STOPPED. F/U ON 09JUN2004 REPORTED THAT EVENTS WERE DUE TO SIADH (NOT FURTHER SPECIFIED). PT WAS CONSIDERED COMPLETELY RECOVERED BY 20JUN2004.

Dept. Tracking Notes/Info: *[unanswered]*

Case Safety Report Number: PHHO2004CH08153

Fatality: No

Suspect Drugs: A drug was involved with this event. See below.

Patient

Initials: *[unanswered]* Age: 35 Gender: Female

Number: *[unanswered]* Height: *[unanswered]* Race: *[unanswered]*

Adverse Event Terms (MedDRA)

- | | | |
|---|--|--|
| 1 | PT: Inappropriate antidiuretic hormone secretion | Relationship: Probable (from external investigator)
Inconclusive (Possible) (from sponsor) |
| | SOC: Endocrine disorders | Severity: 3 - Severe |
| 2 | PT: Hyponatraemia | Relationship: Inconclusive (Possible) (from external investigator)
Inconclusive (Possible) (from sponsor) |
| | SOC: Metabolism and nutrition disorders | Severity: 2 - Moderate |



Occurrences and Changes Necessitated by Event

- No Has the event occurred before **at your institution** on this protocol?
- 0 How many times has this event occurred at Georgetown on this protocol?
- No Has the event occurred before at a site **other than your institution** on this protocol?
- 0 How many times has the event occurred at a site other than Georgetown on this protocol?
- 0 How many times has the event occurred at a site other than Georgetown on any protocol other than this one?
- Yes Is the risk of this reaction listed in the protocol?
- No Is the risk of this reaction listed in the Informed Consent Form (ICF)?
- No Are changes to the protocol required?
[no rationale supplied]
- No Are changes to the ICF required?
Rationale: MENTAL IMPAIRMENT (CONFUSION) IS LISTED IN CONSENT, SIADH AND HYPONATREMIA ARE NOT BUT CAUSALITY ARE SUSPECT IN LIGHT OF PATIENTS HISTORY OF THYROID DISORDER



Amendments

1 Sorell L. Schwartz, Chairman, IRB Subcommittee on Adverse Events

Tuesday 10/05/2004

Because the external investigator assessed the causal relationship as "probable" we are obligated to act on that judgment unless there is a compelling reason to do otherwise. Though there is a plausible alternative cause, it is insufficient reason to disregard the external investigator's judgment.

Revise ICF to include SIADH and hyponatremia.

Continue. Submit revised ICF to IRB office along with a hardcopy of this report.

Requires modification

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Amendments

- 1 Sorell L. Schwartz, Chairman, IRB Subcommittee on Adverse Events Monday 09/13/2004
Provide details as to the nature of ECG changes.
Continue
Response required by clicking the "Amend" button
- 2 [Respondent's name redacted] Tuesday 09/14/2004
The initial reading of ECG showed "abnormal left axis deviation, high chest lead placement unless clinical evidence of heart or lung disease. Poor anterior R progression. Possible anterolateral ischemia." Dr. [redacted] has seen this ECG and states "leftward axis and diffuse STT abnormality" based only upon this ECG (small machine, transmission over phone lines). He intends to repeat this ECG at his office at the time of consult.
- 3 Sorell L. Schwartz, Chairman, IRB Subcommittee on Adverse Events Tuesday 09/14/2004
Contact sponsor's study monitor by phone, email, or fax to determine if ECG changes have been observed in other patients, and, if so the nature of the changes. The request is for observed incidents --- not incidents that have necessarily been determined to be asoprinisil caused.
Continue
Response required by clicking the "Amend" button
- 4 [Respondent's name redacted] Tuesday 09/14/2004
We have had 5 patients here at Georgetown that have had cardiology consults. None of these patients have actually had clinically significant changes on repeat ECG's using a larger, more sensitive machine. Perhaps I am being hasty in filing this AE report without knowing if this is truly a clinically significant change? It is suspected that these changes are related to the smaller machine and/or transmission of the data over phone lines. Dr. [redacted] does repeat the ECG in his office at the time of consult. Does this help? I will gather more information if needed. Thank you!
- 5 Sorell L. Schwartz, Chairman, IRB Subcommittee on Adverse Events Tuesday 09/14/2004
The concern is that some of the most unexpected but relevant and serious adverse drug reactions relate to cardiac arrhythmogenicity. We will await your follow up.
Continue
Noted. No further action required
- 6 [Respondent's name redacted] Wednesday 10/06/2004
Happily, we can report that Dr. [redacted] found no clinically significant cardiac problems in this patient. She has had an echocardiogram, repeat ECG and consultation without problems. She is continuing in the study.
- 7 Sorell L. Schwartz, Chairman, IRB Subcommittee on Adverse Events Wednesday 10/06/2004
Continue
Noted. No further action required

Axis A - Qualitative Plausibility

Can the study drug(s) cause the observed event?

- Grade 1:** The adverse event is widely known and accepted as an effect of (or response to) one or more of the drugs in the study.
- Grade 2:** There are sufficient human and/or experimental animal data to support the inference that the adverse event can be caused by one or more of the drugs in the study.
- Grade 3:** Based on current general knowledge, the event is a biologically plausible response to the one or more of the study drug, though data from human and/or experimental animal studies are indecisive.
- Grade 4:** Based on current general knowledge, the event is not a biologically plausible response to the study drug(s) OR there are data that actually refute that inference that the adverse event can be caused by the study drug(s).

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Axis B: Timing

- Grade 1:** The **timing** of the adverse event is consistent with past observations with the suspected study drug(s) or is otherwise to be expected for this adverse event.
- Grade 2:** The association between the suspected study drug(s) and the response is so unusual as to prevent knowing what **timing** to expect for a reaction of this type.
- Grade 3:** The **timing** is inconsistent with a response caused by the suspected study drug(s).

Next ->



Axis C: Dose - Response

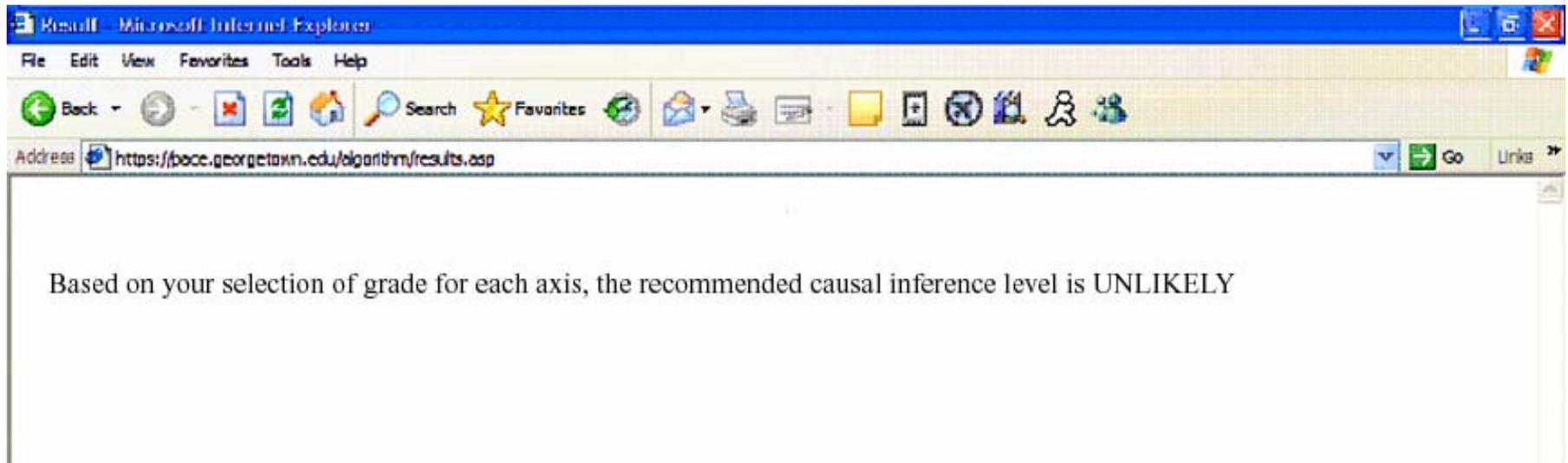
- Grade 1:** The dose-response data are consistent with adverse events associated with the suspected study drug(s).
- Grade 2:** The response is not normally dose related (e.g., an immunologically-mediated reaction) OR there is inadequate dose-response information available to make an Grade.
- Grade 3:** The dose-response data are not generally recognized as consistent with an adverse response to the suspected study drug(s).

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Axis D: Alternative Hypotheses Non-Drug Causation

- Grade 1:** Other plausible candidates have been eliminated. (Note: Where a particular health disturbance is commonly of unknown etiology, then "unknown etiology" can be considered as a candidate plausible alternative).
- Grade 2:** Any other plausible explanations of the adverse event, including the known course of the underlying disease, if not eliminated, are assessed to be less likely causal explanations than the study drug regimen.
- Grade 3:** In light of the patient's condition and the study conditions, the response commonly occurs in the presence of other factors characteristic of this study.
- Grade 4:** A cause other than the study drug(s) is considered to be more likely than not the cause of the adverse event.

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CAER – Status

- Beta testing began April 2003
- Incrementally rolled out to GU and Non-GU departments, under the oversight of GU IRB and MedStar Research Institute - Georgetown University Joint Oncology Institutional Review Board
- November 1, 2004: Full rollout; paper-based AE report forms no longer accepted



Snapshot

- From first use, April 2003 to 3/15/2005, the total number of CAER reports = 2612
 - 304 (11.6%) of these were internal; 22 of these led to ICF revisions
 - 2308 (88.4%) were external events; 533 of these led to ICF revisions



Snapshot

- Between 11/01/2004 to 3/15/2005 present, the total number of CAER reports = 777
 - 97 (12.5%) of these were internal: 3 of these led to ICF revision
 - 680 (87.5%) were external events: 161 were filed as "expected"
 - 145 ICF revisions were required as a result of external AE reports

