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Adverse Events (Part 8 of Safety and Efficacy of Imatinib for Preserving Beta-Cell Function in New-onset Type 1 Diabetes Mellitus)

In 1 collection

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ABSTRACT

This is Part 8 of "Safety and Efficacy of Imatinib for Preserving Beta-Cell Function in New-Onset Type 1 Diabetes Mellitus".

This clinical study is supported by JDRF. The aim of the collection is to determine whether imatinib will slow the progression of the autoimmune destruction of ß cells and lead to the preservation of C-peptide secretion in T1DM and to assess Diabetes-related objectives and safety of Imatinib in new-onset type 1 diabetes mellitus".

ATTACHMENTS

dngubkeaf.pdf

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COLLECTIONS

Collection of Protocols and Guidelines for Safety and Efficacy of Imatinib for Preserving Beta-cell Function in New-onset Type 1 Diabetes Mellitus

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GUIDELINES

8.1 ADVERSE EVENT DEFINITION

8.1.1 Adverse Event

In this clinical trial, an adverse event is any occurrence or worsening of an undesirable or unintended sign, symptom or disease whether or not associated with the treatment and study procedures.

Throughout the study, the investigator must record all adverse events on source documents. Events not related to hypo or hyperglycemia that are Grade 2 or greater per the NCI CTCAE 4.0 (see Section 8.1.4. Grading Event Severity below) must be reported to the Coordinating Center on the appropriate adverse event form. The investigator should treat participants with adverse events appropriately and observe them at suitable intervals until the events resolve or stabilize.

Adverse events may be discovered through:

- observation of the participant;
- questioning the participant;
- unsolicited complaint by the participant

In questioning the participant the questioning should be conducted in an objective manner.

An abnormal value or result from a clinical or laboratory evaluation (e.g., a radiograph, an ultrasound, or an electrocardiogram) can also indicate an AE if it is determined by the investigator to be clinically significant. If this is the case, it must be recorded in the source document and as an AE on the appropriate AE form(s). The evaluation that produced the value or result should be repeated until that value or result returns to normal or can be explained and the participant's safety is not at risk.

8.1.2 Serious Adverse Event

For this trial, an adverse event associated with the treatment or study procedure that suggests a significant hazard, contraindication, side effect or precaution (as described below) is to be reported as a serious adverse event (SAE). A serious adverse event (experience) or reaction is any untoward medical occurrence that:

- results in death,
- is life-threatening,
- requires inpatient hospitalization or prolongation of existing hospitalization,
- results in persistent or significant disability/incapacity, or
- is a congenital anomaly/birth defect.

Important medical events that may not result in death, be life threatening, or require hospitalization may be considered serious adverse events when, based upon appropriate medical judgment, they may jeopardize the patient and may require medical or surgical intervention to prevent one of the outcomes listed above.

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8.1.3 Unexpected Adverse Event

An adverse event is considered unexpected when the nature (specificity) or severity of the event is not consistent with the risks described in the protocol or informed consent document for a particular protocol.

8.1.4 Grading Event Severity

This study has adopted usage of the National Cancer Institute (NCI) Common Technology Criteria for Adverse Events (CTCAE) version 4.0 and/or study-specific criteria for classification to describe the severity of adverse events with the exception of hyper and hypoglycemia. For this study, a reportable hypoglycemic event is defined as those resulting in loss of consciousness, seizure, or requiring assistance of others due to altered state of consciousness and hyperglycemic event is one resulting in DKA.

Adverse events will be graded on a scale from 1 to 5 according to the following standards in the NCI-CTCAE manual:

• Grade 1 = mild adverse event.
• Grade 2 = moderate adverse event.
• Grade 3 = severe and undesirable adverse event.
• Grade 4 = life-threatening or disabling adverse event.
• Grade 5 = death.

For additional information and a printable version of the NCI-CTCAE manual, go to
http://ctep.cancer.gov/reporting/ctc.html

8.1.5 Attribution Definitions

Adverse events will be categorized for their relation to imatinib. The investigator will determine the relation, or attribution, of an AE to study participation and will record the determination on the appropriate CRF and/or SAE reporting form. The relation of an AE to study participation will be determined using definitions in Table 1.

Table 1. Attribution of adverse events

Code	Descriptor	Definition
Unrelated Category		
1	Unrelated	The adverse event is *clearly* not related.
Related Categories		
2	Unlikely	The adverse event is *doubtfully* related.
3	Possible	The adverse event *may be* related.
4	Probable	The adverse event is *likely* related.
5	Definite	The adverse event is *clearly* related.

8.2 ADVERSE EVENT REPORTING AND MONITORING

Study personnel will assess adverse events and the use of concomitant medications throughout the study. Adverse events will be reported to the Coordinating Center as described below. They will be graded as to severity according to common toxicity criteria or study-specific criteria and the investigator will make a determination as to the relation to therapy. Events will be assessed and reported in accordance with the ICH Guideline For Good Clinical Practice and per the guidance of the DHHS Office for Human Research Protections (OHRP). The adverse event case report form for the protocol must be completed for all adverse events (AE) of Grade 2 or greater severity regardless of relationship to therapy. For reporting serious adverse events (SAE), the MedWatch Form should also be completed and faxed to the Coordinating Center within 24 hours of when the site was notified of the event. This will be reviewed by the study Safety Monitoring Committee, and the Data and Safety Monitoring Board (DSMB) as appropriate. Deaths must be reported immediately. Event outcome and other follow-up information regarding the treatment and resolution of the event will be obtained and reported when available, if not known at the time the event is reported. The follow-up information should contain sufficient detail to allow for

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a complete medical assessment of the case and an independent determination of possible causality.

Adverse events will be assessed by the study designated Medical Monitor. The DSMB will conduct regular safety reviews approximately every three to six months (and, as needed) of adverse events by treatment group assignment. Serious adverse events as well as adverse events leading to treatment discontinuation will be reviewed by the DSMB.

8.2.1 Reporting Pregnancy

The investigator should be informed immediately of any pregnancy. At each visit the investigator will determine the pregnancy status of female participants and that the sexual partners of male participants. Pregnancy information should be entered into the electronic data capture (EDC) system within 24 hours of becoming aware of the event. The investigator should counsel the participant and discuss the risks of continuing with the pregnancy and the possible effects on the fetus. Monitoring of the participant should continue until the conclusion of the pregnancy. Follow-up information detailing the outcome of the pregnancy should be entered into the EDC system as it becomes available. Any premature termination of the pregnancy will be reported.

While pregnancy itself is not considered to be an AE or SAE, any pregnancy complication or elective termination of a pregnancy for medical reasons will be recorded as an AE or SAE as described in sections 8.2.1 and 8.2.2.

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