COG-ALTE03N1: Key Adverse Events after Childhood Cancer

FAST FACTS
Eligibility Reviewed and Verified By
_____ MD/DO/RN/LPN/CRA Date _____
_____ MD/DO/RN/LPN/CRA Date _____
Consent Version Dated_____

PATIENT ELIGIBILITY:
Important note: The eligibility criteria listed below are interpreted literally and cannot be waived (per COG policy posted 5/11/01).
Cases will consist of **patients experiencing a key adverse event,** who meet the following criteria:

___1. Diagnosis of primary cancer at age 21 or younger, irrespective of current age
___2. No prior history of allogeneic (non-autologous) hematopoietic cell transplant
___3. Development of one of the following key adverse events at any time following initiation of cancer therapy (see section 4.1 for definitions):
- Ischemic stroke (IS)
- Subsequent malignant neoplasm (SMN)

___4. Submission of a blood specimen (or in certain cases a buccal cell specimen) to the Clinical Pharmacokinetics Laboratory at St. Jude Children's Research Hospital as per the requirements outlined in section 4.4.*
**Please Note: If a patient is currently receiving active cancer treatment, it is preferable to obtain the blood sample at a time when the patient's WBC is >2,000*
___5. Written informed consent from the patient and/or the patient's legally authorized guardian.
___6. In active follow up by a COG institution.

Active follow up will be defined as date of last visit or contact by a COG institution within the past 24 months. Any type of contact, *including contact specifically for participation in ALTE03N1*, qualifies as active follow-up.

Please Note: Treatment on a COG (or legacy group) therapeutic protocol for the primary cancer is NOT required.

Eligibility criteria for controls:

___1. Diagnosis of primary cancer at age 21 or younger, irrespective of current age
___2. No prior history of allogeneic (non-autologous) hematopoietic cell transplant
___3. **No clinical evidence** of any of the following key adverse events:
- Cardiac dysfunction (CD)*
- Myocardial infarction (MI)
- Ischemic stroke (IS)
- Avascular necrosis (AVN)
- Subsequent malignant neoplasm (SMN)

___4. Submission of a blood specimen (or in certain cases a buccal cell specimen) to the Clinical Pharmacokinetics Laboratory at St. Jude Children's Research Hospital as per the requirements outlined in section 4.4.
**Please Note: If a patient is currently receiving active cancer treatment, it is preferable to obtain the blood sample at a time when the patient's WBC is >2,000.*
___5. Written informed consent from the patient and/or the patient's legally authorized guardian, obtained in accordance with institutional policies approved by the U.S. Department of Health and Human Services.
___6. In active follow up by a COG institution.

Active follow up will be defined as date of last visit or contact by a COG institution within the past 24 months. Any type of contact, *including contact specifically for participation in ALTE03N1*, qualifies as active follow-up.

Please Note: Treatment on a COG (or legacy group) therapeutic protocol for the primary cancer is NOT required.

For both groups:

___1. Submission of a blood specimen (or in certain cases a buccal cell specimen) to the Clinical Pharmacokinetics Laboratory at St. Jude Children's Research Hospital as per the requirements outlined in section 4.4.*
**Please Note: If a patient is currently receiving active cancer treatment, it is preferable to obtain the blood sample at a time when the patient's WBC is >2,000.*

___2. Cardiac dysfunction (CD)
Cardiac dysfunction will be defined as follows:
- **Symptomatic Cardiac Dysfunction** – current or previous diagnosis of congestive heart failure (based on clinical criteria such as pulmonary and/or peripheral edema, dyspnea, orthopnea, fatigue, hepatomegaly).
  OR
- **Asymptomatic Cardiac Dysfunction** defined as ejection fraction <40% on echocardiogram or MUGA and/or fractional shortening <28% on echocardiogram without clinical symptoms.

___3. Myocardial infarction (MI) **(case enrollment closed as part of amendment #3)**
Criteria used in the WHO monitoring of trends and determinants in cardiovascular disease (MONICA) will be used.200 MI will be defined as:
- Definite ECG changes; **OR**
- symptoms, typical/ atypical/ inadequately described + probable ECG + abnormal enzymes including creatine kinase MB; **OR**
- symptoms, typical + abnormal enzymes including creatine kinase MB + ischemic ECG/ non-codable ECG/ ECG not available.

___4. Ischemic Stroke (Stroke)
Ischemic stroke will be defined as:
- A fixed neurologic deficit lasting for more than 24 hours, **AND**
- Confirmation by a computed tomography or magnetic resonance imaging scan within seven days of onset of symptoms.

Subarachnoid and intracerebral hemorrhage, transient ischemic attacks, and amaurosis fugax will be excluded.

___5. Avascular Necrosis (AVN) **(case enrollment closed 3/24/2006 due to target accrual achievement, then re-opened as part of Amendment #5, to allow for accrual of additional patients who have not received an allogeneic (non-autologous) transplant.)**
Diagnosis of avascular necrosis will be made by:
- Clinical symptoms of joint pain, joint stiffness, or decreased range of motion **AND**
- Radiographic confirmation (e.g. plain radiographs, computerized tomography, magnetic resonance imaging, bone scan)

___6. Subsequent Malignant Neoplasm (SMN)
Subsequent malignant neoplasms will be defined as:
- Histologically distinct neoplasms developing in patients treated for a primary cancer, **AND**
- Institutional pathology report confirming diagnosis of SMN

REQUIRED OBSERVATIONS:
No specific pre-study observations required.

TREATMENT PLAN:
This is a data collection study

TOXICITIES AND DOSAGE MODIFICATIONS:
None

SPECIMEN REQUIREMENTS:
Blood (6 ml) for DNA will be collected into a special plastic "purple-top" EDTA tube (supplied in kit). Blood (2.5 ml) for RNA will be collected into a PAX gene blood RNA tube (supplied in kit). *Please Note: If a patient is currently receiving active cancer treatment, it is preferable to obtain the blood sample at a time when the patient's WBC is >2,000.*

Subjects who are unable or unwilling to provide a blood specimen will be asked to provide a buccal cell sample.