SAFETY

Surveillance After Extremity Tumor Surgery

Patient Screening and Eligibility Guidelines

Version 2.0

This study is registered on ClinicalTrials.gov
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Document History

Date (DD-MMM-YY)	Author(s)	Version No.	Description of Amendment(s)
26-MAY-20	Tricia Schneider	1.0	Initial Version
11-JAN-22	Tess Hudson	2.0	▪ Updated screening procedures to specify that only patients that have undergone surgery with curative intent should be screened. ▪ Removed an exclusion criterion (The patient has been diagnosed with another malignancy in the last five years). ▪ Added section on following non-local patients. Added common questions to FAQ section.

1.0 Introduction

The purpose of this document is to provide guidance on patient eligibility and screening for the **S**urveillance **AF**ter **E**xtremity **T**umor surger**Y** (SAFETY) trial. Clinical site personnel should review this document prior to beginning study recruitment and refer to it when questions arise. If clinical site personnel have questions regarding patient eligibility, they should contact the Project Manager at the Methods Center via email and / or telephone.

2.0 Patient Identification

The management of sarcoma patients can vary between sites with respect to post-operative chemotherapy and / or radiation. Therefore, patients will become eligible for screening at the first clinic visit at which: A) all treatment is complete; B) the surgical wound is deemed healed or stable; and C) the plan for post-treatment surveillance is discussed with the patient. Clinical site personnel will screen all patients 18 years of age or older who present to a participating site with an extremity soft-tissue sarcoma (STS) for participation in the SAFETY trial. This process may include:

- Participation in daily / weekly sarcoma patient rounds;
- Review of daily listing of hospital admissions for STS patients;
- Reminder of open recruitment for the study at weekly hospital staff meetings; or
- Review of clinic listings for patients who are presenting to clinic after surgery.

Clinical sites can also continue to follow their usual screening practices that have been successful in previous trials. However, the screening and consent processes must take place prior to the patient entering a period of surveillance.

3.0 Eligibility Criteria

Once clinical site personnel identify a patient 18 years of age or older with a primary extremity STS who has undergone surgical excision of the tumor with curative intent, they will apply the eligibility criteria as part of the screening process. If the patient meets any of the criteria below, they should be considered ineligible:

- The patient has *not* been diagnosed with an extremity grade II or III STS;
- The patient has *not* undergone surgical excision of the tumor with curative intent;
- The patient underwent surgical management of the tumor at a non-participating hospital or clinic;
- The patient's tumor is *not* greater than or equal to (≥) five centimeters according to the pathology report (or the pre-treatment MRI if neoadjuvant radiation and / or chemotherapy were given);
- The patient has metastases at initial presentation based on the radiology report of the initial thoracic imaging or at the time of the restaging chest CT scan upon completion of local treatment;
- The patient has recently undergone surgical excision of a local recurrence;
- The patient has been diagnosed with one of the special sub-types, myxoid / round cell liposarcoma or extra-skeletal Ewing's sarcoma;

- The patient has been previously diagnosed with a genetic syndrome with an elevated risk of malignancy, such as Li-Freumeni Syndrome;
- The patient has been previously diagnosed with a co-morbid condition that has a life expectancy of less than (<) one year;
- The site-specific surveillance protocol for the patient's disease is not compatible with the study protocol (i.e., regular planned whole-body imaging with positron emission tomography [PET] scans);
- There are likely problems, in the judgment of the investigator, with maintaining patient follow-up;
- The patient is currently enrolled in a study that does not permit co-enrolment; or
- The patient was already previously enrolled in the SAFETY trial.

The reason(s) for exclusion should be documented on a Screening Form.

4.0 Submission of Screening Forms

Screening data should be submitted to the Methods Center by completing the Screening Form in the iDataFax electronic data capture (EDC) system being used in this study.

5.0 Classification of Patients

All screened patients should be classified as one of the following three classifications:

1. **Eligible and INCLUDED:** Include in the trial all patients 18 years of age or older with a primary extremity STS who have undergone surgical excision of the tumor with curative intent and who meet the inclusion criteria (including the provision of consent) and are free from the exclusion criteria.
2. **Ineligible and EXCLUDED:** Exclude from the trial all patients 18 years of age or older with a primary extremity STS who have undergone surgical excision of the tumor with curative intent and who meet one or more of the exclusion criteria or do not meet one or more of the inclusion criteria.
3. **MISSED:** Record as "missed" all patients who were not screened prior to the commencement of post-operative surveillance but were otherwise eligible for the trial.

6.0 Screening Procedures

Screening Forms should be completed for **all** patients 18 years of age or older who present to a participating clinical site for treatment and surveillance of a primary extremity STS that was treated with surgery with curative intent. Screening Forms are **not** required for patients who do not have a primary extremity STS or who are younger than 18 years of age or who did not undergo surgery with curative intent. A Screening Form is not required for patients 18 years of age or older who present with a primary extremity STS if it will be conservatively or palliatively managed instead of surgically.

Examples:

- A 17-year-old patient presents to a participating clinical site with a primary extremity STS, a Screening Form is not required as the patient is younger than 18 years of age.

- An 18-year-old patient presents to a participating clinical site with a STS that did not originate in an extremity, a Screening Form is not required because the patient does not have a primary extremity STS. *Note*: If you are unsure if the tumor is located in an extremity and/or should be included in the trial, please contact the Methods Centre for verification.
- A 70 year-old patient presents to a participating clinical site with a primary extremity STS, but does not undergo surgery, a Screening Form is not required because the patient did not undergo surgery with curative intent.

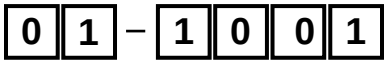
Once a Screening Form has been completed, a Participant ID should be assigned for the patient. For eligible and included patients this number will be automatically generated in the Randomization system. For ineligible and excluded patients and missed patients, the number must be provided in sequence by research personnel as described below. The Participant ID format looks like this:

It consists of three parts:

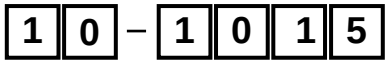
- The first two digits are set by the Methods Center and designate the participating clinical site ID. All patients screened by the same participating clinical site will have the same first two digits.
- The third digit (immediately after the dash) designates the classification of the patient. All included patients will use “1”, missed patients will use “2” and excluded patients will use “3” as the third digit.
- The last three digits are designated in sequential order, beginning with “001”.

Therefore:

- The **first** included patient at Site 01 will have a Participant ID of:



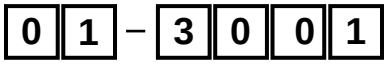
- The **fifteenth** included patient at Site 10 will have a Participant ID of:



- The **first** missed patient at Site 01 will have a Participant ID of:

- The **tenth** missed patient at Site 10 will have a Participant ID of:

- The **first** excluded patient at Site 01 will have a Participant ID of:



- The **fifth** excluded patient at Site 10 will have a Participant ID of:

7.0 Frequently Asked Questions

This section provides clarification and guidance on the application of the study eligibility criteria as well as the screening procedures. Please contact the Methods Center if you have any questions about a particular patient's eligibility for the trial.

7.1 Is there a maximum age?

There is no upper age limit unless required by local regulations.

7.2 What if our local regulations require a different minimum age?

Some participating clinical sites may have local or national regulations governing the minimum age for participation in a randomized controlled trial, so they may receive approval from the Methods Center to modify the minimum age of inclusion.

7.3 Can patients with dementia be included in the trial?

Please exclude patients with frank dementia that will interfere with collecting the primary outcome at five years, based on the site investigator's clinical judgment or according to local regulations, if applicable. Patients with mild to moderate dementia should be included provided the consent process can be completed according to local regulations. If permissible by local regulations, a legal authorized representative may provide consent for the patient to participate, and the patient should provide assent. It is acceptable to have a supportive family member or friend available to assist with filling out questions regarding medical history or events, so patients with mild or moderate dementia should be included whenever possible. However, family friends and friends should not answer questionnaires on behalf of the patient.

7.4 What if we anticipate that a patient will be difficult to follow for five years?

Please exclude patients if they do not have a permanent address or are expected to move and will be unable to continue follow-up. If a patient unexpectedly moves, you may obtain permission from the patient to continue study follow-up via telephone, email, or text. If a patient happens to move his or her STS care to another participating clinical site, you may obtain permission from the Methods Center to transfer the patient's follow-up to the other participating clinical site.

7.5 What if a patient is unable to obtain imaging and attend follow-up appointments locally?

A patient may obtain imaging at an outside medical imaging facility provided the patient's orthopaedic oncologist can obtain the image(s). Follow-up visits may be conducted via phone or teleconference/telemedicine.

7.6 How do we determine if we should exclude a patient who is already enrolled in another trial?

Any patient who is participating in a trial where the follow-up might conflict with either surveillance visit frequencies (i.e., every 3 or every 6 months) should not be included in the trial. Please contact the Methods Center if you have any questions regarding eligibility.

7.7 Can a patient with a language barrier be included?

We are permitting participating clinical sites to enrol patients that have a language barrier so long as the consent process can be completed as per local regulations and the study questionnaires have been translated into the patient's primary language. It is acceptable to have a supportive family member or friend available to assist with filling out case report forms, so these patients should be included whenever possible. However, some participating clinical sites may have difficulty enrolling patients with a language barrier due to local regulations or unavailability of

translation services. If you need to exclude a patient due to a language barrier, please record the reason under “Q15. Is there any other reason to exclude the patient?” on the **Screening Form**.

7.8 Can a patient with indeterminate nodules be enrolled?

Patients with indeterminate nodules may be enrolled in the trial, provided the indeterminate nodules are followed and determined to be stable. Please use Q3. on the Baseline Thoracic Imaging Report Form (Form 3) to record the details, which asks whether indeterminate nodules were found, the number of nodules, and whether they were determined to be stable.

7.9 Can a patient with positive margins be included?

No, patients with positive margins may not be included. However, patients with positive margins that were revised intra-operatively or returned to the operating room to achieve negative margins may be included, provided that the original tumor met the size and grade criteria.

7.10 Can a patient be included in the SAFETY trial more than once?

Patients who were previously enrolled in the SAFETY trial and present with a new primary extremity STS are not eligible for participation again.

7.11 What should be done if a patient is discovered to be ineligible after they have been enrolled?

Patients who are enrolled but are later suspected to be ineligible will stay enrolled in the trial until the Central Adjudication Committee (CAC) determines whether they are eligible or not. Please notify the Methods Center in such situations and submit all available hospital / clinic notes and imaging to the Methods Center as soon as possible. The Methods Center personnel will send these documents to the CAC members for review and will notify the local study team of the CAC’s decision.

If the CAC determines that the participant is eligible, the participant should continue to be followed in the study. If the CAC determines that the participant is ineligible, the participant should be withdrawn from the study and an **Early Withdrawal Form** should be completed. Participants should not be withdrawn until confirmation is received from the Methods Center.