SAFETY

Surveillance After Extremity Tumor Surgery

Study Follow-Up Guidelines

Version 1.0

This study is registered on ClinicalTrials.gov
Identification No.: NCT03944798

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Document History

Date (DD-MMM-YY)	Author(s)	Version No.	Description of Amendment(s)
28-MAY-20	Tricia Schneider & Victoria Giglio	1.0	Initial Version

1.0 Introduction

The purpose of this document is to provide guidance on the trial 'intervention phase' and 'post-intervention phase' follow-up visits 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 enrolment and refer to it when questions arise. If clinical site personnel have questions regarding participant follow-up, they should contact the Project Manager at the Methods Center via email and / or telephone.

2.0 Intervention Phase Visits

Following the completion of active therapy (surgery ± radiation ± systemic treatment), participants will be randomized into the study. Participants will first be randomized to one of the two thoracic imaging modalities being evaluated (i.e., chest radiograph [CXR] vs. chest computed tomography [CT] scan). Participants will then be randomized to one of the two surveillance frequencies being evaluated (i.e., every three months vs. every six months). Therefore, half of all participants will have four post-operative clinic visits per year and half will have two post-operative clinic visits per year for the first two years of the study (called the study 'intervention phase'). As per the National Comprehensive Cancer Network (NCCN) guidelines, both frequencies are consistent with the current standard of care. Therefore, these intervention phase visits may be completed in clinic as part of the standard of care post-operative follow-up appointments. If no visit is scheduled, these visits may be completed by telephone, email, text, mail or an alternate contact provided that the appropriate imaging is still obtained (see the **Study Imaging Guidelines** in the Study Resource Binder). Additional verification of data in the participant's medical records should be completed at each visit.

Table 1 below lists the intervention phase visits and visit windows. The intervention phase visit windows touch so that each visit will fall into a specific window. It is very important that all intervention phase visits are completed to ensure data integrity and reduce the risk of loss to follow-up.

Table 1. Acceptable Intervention Phase Visit Windows

Intervention Phase Visit	Acceptable Visit Window
3-Month Visit	2 – 4 Months
6-Month Visit	5 – 7 Months
9-Month Visit	8 – 10 Months
12-Month Visit	11 – 13 Months
15-Month Visit	14 – 16 Months
18-Month Visit	17 – 19 Months
21-Month Visit	20 – 22 Months
24-Month Visit	23 – 25 Months

2.1 Intervention Phase Visit Forms

See **Table 2** below for a schedule of events at each of the intervention phase visits.

Table 2. Intervention Phase Data Collection Schedule

Data Collection	*Intervention Phase Visits*							
	3M Visit	**6M Visit**	**9M Visit**	**12M Visit**	**15M Visit**	**18M Visit**	**21M Visit**	**24M Visit**
Case Report Forms								
Intervention Phase Surveillance Visit Form (Form 8)	✓*	✓*	✓*	✓*	✓*	✓*	✓*	✓*
PROMIS® Cancer-Anxiety Questionnaire (Form 20)		✓		✓		✓		✓
PROMIS® Satisfaction with Social Roles and Activities Questionnaire (Form 21)		✓		✓		✓		✓
EQ-5D™ Questionnaire (Form 22)		✓		✓		✓		✓
Patient Cancer Care Cost Diary (Form 23)	✓*	✓*	✓*	✓*	✓*	✓*	✓*	✓*
Local Recurrence Form (Form 12)	✦†	✦†	✦†	✦†	✦†	✦†	✦†	✦†
Systemic Recurrence Form (Form 13)	✦†	✦†	✦†	✦†	✦†	✦†	✦†	✦†
Unplanned Re-Operation Form (Form 14)	✦†	✦†	✦†	✦†	✦†	✦†	✦†	✦†
Other Surgical Intervention Form (Form 15)	✦†	✦†	✦†	✦†	✦†	✦†	✦†	✦†
Adverse Event Form (Form 16)	✦†	✦†	✦†	✦†	✦†	✦†	✦†	✦†
Systemic Therapy Log (Form 17)	✦†	✦†	✦†	✦†	✦†	✦†	✦†	✦†
Radiation Log (Form 18)	✦†	✦†	✦†	✦†	✦†	✦†	✦†	✦†
Protocol Deviation Form (Form 19)	✦†	✦†	✦†	✦†	✦†	✦†	✦†	✦†
Imaging								
Chest Radiographs	✓*†	✓*†	✓*†	✓*†	✓*†	✓*†	✓*†	✓*†
Chest CT Scans	✓*†	✓*†	✓*†	✓*†	✓*†	✓*†	✓*†	✓*†

✓ Required
✦ As Needed
* As Per Surveillance Frequency Allocation
† As Per Imaging Modality Allocation

2.1.1 Intervention Phase Surveillance Visit Form

An **Intervention Phase Surveillance Visit Form (Form 8)** must be completed at each intervention phase visit. For guidelines on the completion of this case report form (CRF), please refer to the **Case Report Form Completion Guidelines** in the Study Resource Binder.

2.1.2 Participant Questionnaires

Soft-tissue sarcoma patients are at a high risk for emotional distress and quality of life disruptions, and the frequency of post-operative surveillance may exacerbate these issues. The validated Patient-Reported Outcomes Measurement Information System (PROMIS)® Cancer-Anxiety, the PROMIS® Satisfaction with Social Roles and Activities and the EuroQol-5 Dimension (EQ-5D™) questionnaires will be administered to evaluate the impact of post-operative surveillance

strategies on patient anxiety, overall satisfaction and quality of life. For guidelines on the completion of these participant questionnaires, please refer to the **Case Report Form Completion Guidelines** in the Study Resource Binder.

2.1.2.1 PROMIS® Cancer-Anxiety Questionnaire

The **PROMIS® Cancer-Anxiety Questionnaire (Form 20)** measures self-reported fear (fearfulness, panic), anxious misery (worry, dread), hyperarousal (tension, nervousness, restlessness), and somatic symptoms related to arousal (racing heart, dizziness). This study is utilizing the short-form version of the questionnaire. This questionnaire should be completed by the study participant at the 6-month, 12-month, 18-month and 24-month intervention phase surveillance visits.

2.1.2.2 PROMIS® Satisfaction with Social Roles and Activities Questionnaire

The **PROMIS® Satisfaction with Social Roles and Activities Questionnaire (Form 21)** measures self-reported satisfaction with social roles such as work and family responsibilities, and more discretionary social activities such as leisure activity and relationships with friends. This study is utilizing the short-form version of the questionnaire. This questionnaire should be completed by the study participant at the 6-month, 12-month, 18-month and 24-month intervention phase surveillance visits.

2.1.2.3 EQ-5D™ Questionnaire

The **EQ-5D™ Questionnaire (Form 22)** measures generic health status across five dimensions: mobility, self-care, usual activities, pain / discomfort and anxiety / depression. This questionnaire should be completed by the study participant at the 6-month, 12-month, 18-month and 24-month intervention phase surveillance visits.

2.1.3 Participant Cost Diary

The **Patient Cancer Care Cost Diary (Form 23)** evaluates costs associated with health services used as a result of or related to the participant's sarcoma. A new Patient Cancer Care Cost Diary should be provided to the participant at each visit for him / her to complete at home and return at his / her next visit (irrespective of whether the participant was randomized to every three months or every six months visits). For guidelines on the completion of this CRF, please refer to the **Case Report Form Completion Guidelines** in the Study Resource Binder.

2.1.4 As Needed Forms

In addition to the CRFs listed above, the completion of the following CRFs may also be required:

- Local Recurrence Form;
- Systemic Recurrence Form;
- Unplanned Re-Operation Form;
- Other Surgical Intervention Form;
- Adverse Event Form;
- Systemic Therapy Log;
- Radiation Log; and
- Protocol Deviation Form.

For guidelines on the completion of these CRFs, please refer to the **Case Report Form Completion Guidelines** in the Study Resource Binder.

3.0 Post-Intervention Phase Visits

Following the completion of the intervention phase, participants will continue to be followed in the study for an additional three years (called study 'post-intervention phase'). During the three-year post-intervention phase, participants will be followed at least every six months as per the NCCN guidelines. Therefore, these intervention phase visits may also be completed in clinic as part of the standard of care post-operative follow-up appointments. If no visit is scheduled, these visits may be completed by telephone, email, text or mail provided that the appropriate imaging is still obtained (see the **Study Imaging Guidelines** in the Study Resource Binder). Additional verification of data in the participant's medical records should be completed at each visit.

Table 3 below lists the post-intervention phase visits and visit windows. The intervention phase visit windows touch so that each visit will fall into a specific window. It is very important that all intervention phase visits are completed to ensure data integrity and reduce the risk of loss to follow-up.

Table 3. Acceptable Post-Intervention Phase Visit Windows

Post-Intervention Phase Visit	Acceptable Visit Window
30-Month Visit	27 – 33 Months
36-Month Visit	34 – 39 Months
42-Month Visit	40 – 45 Months
48-Month Visit	46 – 51 Months
54-Month Visit	52 – 57 Months
60-Month Visit	60+ Months

3.1 Post-Intervention Phase Visit Forms

See **Table 4** below for a schedule of events at each of the post-intervention phase visits.

3.1.1 Post-Intervention Phase Surveillance Visit Form

A **Post-Intervention Phase Surveillance Visit Form (Form 9)** must be completed at each post-intervention phase visit. For guidelines on the completion of the Post-Intervention Phase Surveillance Visit Form, please refer to the **Case Report Form Completion Guidelines** in the Study Resource Binder.

3.1.2 Participant Questionnaires

The validated PROMIS® Cancer-Anxiety, the PROMIS® Satisfaction with Social Roles and Activities and the EuroQol-5 Dimension (EQ-5D) questionnaires will also be administered to study participants at the 36-month, 48-month and 60-month post-intervention phase surveillance visits. For guidelines on the completion of these participant questionnaires, please refer to the **Case Report Form Completion Guidelines** in the Study Resource Binder.

3.1.3 Participant Cost Diary

A new Patient Cancer Care Cost Diary should be provided at each visit for the participant to complete at home and return at his / her next visit. For guidelines on the completion of this CRF, please refer to the **Case Report Form Completion Guidelines** in the Study Resource Binder.

3.1.4 As Needed Forms

In addition to the CRFs listed above, the completion of the following CRFs may also be required:

- Local Recurrence Form;
- Systemic Recurrence Form;
- Unplanned Re-Operation Form;
- Other Surgical Intervention Form;
- Adverse Event Form;
- Systemic Therapy Log; and
- Radiation Log.

For guidelines on the completion of these CRFs, please refer to the **Case Report Form Completion Guidelines** in the Study Resource Binder.

Table 4. Post-Intervention Phase Data Collection Schedule

Data Collection	***Post-Intervention Phase Visits***					
	30M Visit	**36M Visit**	**42M Visit**	**48M Visit**	**54M Visit**	**60M Visit**
Case Report Forms						
Post-Intervention Phase Surveillance Visit Form (Form 9)	✓	✓	✓	✓	✓	✓
PROMIS® Cancer-Anxiety Questionnaire (Form 20)		✓		✓		✓
PROMIS® Satisfaction with Social Roles and Activities Questionnaire (Form 21)		✓		✓		✓
EQ-5D™ Questionnaire (Form 22)		✓		✓		✓
Patient Cancer Care Cost Diary (Form 23)	✓	✓	✓	✓	✓	✓
Local Recurrence Form (Form 12)	✦	✦	✦	✦	✦	✦
Systemic Recurrence Form (Form 13)	✦	✦	✦	✦	✦	✦
Unplanned Re-Operation Form (Form 14)	✦	✦	✦	✦	✦	✦
Other Surgical Intervention Form (Form 15)	✦	✦	✦	✦	✦	✦
Adverse Event Form (Form 16)	✦	✦	✦	✦	✦	✦
Systemic Therapy Log (Form 17)	✦	✦	✦	✦	✦	✦
Radiation Log (Form 18)	✦	✦	✦	✦	✦	✦
Imaging						
Thoracic Imaging (Chest Radiograph OR Chest CT Scan)	✓	✓	✓	✓	✓	✓

✓ Required ✦ As Needed

4.0 Unscheduled Surveillance Visit

4.1 Intervention Phase Unscheduled Surveillance Visits

As per the study protocol, a participant may schedule an ad hoc visit anytime he / she is concerned, even if it breaks the surveillance protocol to which he / she was assigned. Should a participant attend clinic for an unscheduled surveillance visit during the study intervention phase (i.e., anytime during the first two years of the study), an **Unscheduled Surveillance Visit Form (Form 11)** AND a **Protocol Deviation Form (Form 19)** should be completed. For guidelines on the completion of these CRFs, please refer to the **Case Report Form Completion Guidelines** in the Study Resource Binder.

4.2 Post-Intervention Phase Unscheduled Surveillance Visits

Following the completion of the intervention phase, participants will continue to be followed in the study at least every six months for an additional three years during the study post-intervention phase. As per the study protocol, a participant may schedule an ad hoc visit anytime he / she is concerned. Should a participant attend clinic for an unscheduled surveillance visit during the post-intervention phase (i.e., anytime during the final three years of the study), an **Unscheduled Surveillance Visit Form (Form 11)** should be completed. For guidelines on the completion of this CRF, please refer to the **Case Report Form Completion Guidelines** in the Study Resource Binder. As the post-intervention phase is not part of the study intervention, a **Protocol Deviation Form (Form 19)** is NOT required.

5.0 Data Quality & Participant Retention

To maintain the integrity of the SAFETY trial, maintaining data quality and achieving high rates of participant retention are imperative. To improve data quality:

- Ensure that adequate research personnel are assigned to the trial;
- Provide in-services for participating surgeons and sarcoma clinic personnel;
- Prospectively collect data;
- Do not miss visits;
- Use direct data entry into the study database; and
- Ensure vacation / absentee coverage is in place.

Participant retention is also imperative to the success of any trial, as high loss to follow-up threatens the validity of the trial. To reduce the risk of loss to follow-up:

- Complete the **SAFETY Patient Contact Form (Form 0)** with full contact information (including email address) for the participant and three alternate contacts, and confirm that this information is accurate at each study visit;
- Provide participants with your contact information and ask them to contact you if their contact information has changed (i.e., if they have a new phone number or have moved);
- Maintain frequent contact via phone, text, mail or email with participants;
- Contact participants via their preferred method of contact;
- Ask participants to notify you if they will be in clinic; and
- Check medical records for upcoming appointments.

Some strategies for re-establishing contact with a participant who may be lost include:

- Contact the participant's alternate contacts as listed on the **SAFETY Patient Contact Form (Form 0)**;
- Try to contact the participant outside of normal business hours;
- Leave a detailed and clear voice message with your name, contact information and the best time / way to reach you; and
- Search online directories for new contact information.

It is important to be persistent but mindful of the participants' right to withdraw from the study at any time.

5.1 Intervention Phase Missed Surveillance Visits

If a participant is unable to be contacted for a study visit during the intervention phase (i.e., the first two years of the study), a **Missed Surveillance Visit Form (Form 10)** AND a **Protocol Deviation Form (Form 19)** should be completed to indicate why the visit was missed. For guidelines on the completion of these CRFs, please refer to the **Case Report Form Completion Guidelines** in the Study Resource Binder

Visits should only be considered missed if the participant was unable to be contacted during the entire visit window. The Methods Center will closely monitor the submission of Missed Visit Forms and may escalate to the study's Principal Investigator should a high number for any one participant / site be submitted.

5.2 Post-Intervention Phase Missed Surveillance Visits

If a participant is unable to be contacted for a study visit during the post-intervention phase (the final three years of the study), a **Missed Surveillance Visit Form (Form 10)** should be completed, indicating why the visit was missed. For guidelines on the completion of this CRF, please refer to the **Case Report Form Completion Guidelines** in the Study Resource Binder. As this follow-up period is not part of the study intervention, a **Protocol Deviation Form (Form 19)** is NOT required.

Visits should only be considered missed if the participant was unable to be contacted during the entire visit window. The Methods Center will closely monitor the submission of Missed Visit Forms and may escalate to the study's Principal Investigator should a high number for any one participant / site be submitted.