SAFETY

Surveillance After Extremity Tumor Surgery

Study Imaging Guidelines

Version 1.0

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Document History

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1-JUN-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' thoracic imaging 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 thoracic imaging, they should contact the Project Manager at the Methods Center via email and / or telephone.

2.0 Intervention Phase Thoracic Imaging

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 chest radiographs (plain chest x-ray [CXR]) taken and half will have chest CT scans taken for the first two years of the study (called the study 'intervention phase'). Of those having CXRs taken, half will have them taken every three months and half will have them taken every six months for the intervention phase. Of those having chest CT scans taken, half will have them taken every three months and half will have them taken every six months for the intervention phase. See **Table 1** below for the thoracic imaging schedule at each of the intervention phase visits. As per the National Comprehensive Cancer Network (NCCN) guidelines, both thoracic imaging modalities obtained every three to six months is consistent with the current standard of care for soft-tissue sarcoma (STS) patients. Therefore, these thoracic images may be obtained as part of the standard of care post-operative follow-up appointments. It is possible for a participant to obtain his / her thoracic imaging at an outside location provided that the clinical site personnel can obtain a copy of these images and the appropriate clinical assessment is still conducted during a post-operative surveillance visit (see **Study Follow-Up Guidelines** in the Study Resource Binder).

Details of the participant's thoracic imaging will be recorded on the **Intervention Phase Surveillance Visit Form (Form 8)**. For guidelines on the completion of this CRF, please refer to **Case Report Form Completion Guidelines** in the Study Resource Binder.

Table 1. Intervention Phase Thoracic Imaging Schedule

Data Collection	***Intervention Phase Visits***							
	3M Visit	**6M Visit**	**9M Visit**	**12M Visit**	**15M Visit**	**18M Visit**	**21M Visit**	**24M Visit**
Imaging								
Chest Radiographs	✓*†	✓*†	✓*†	✓*†	✓*†	✓*†	✓*†	✓*†
Chest CT Scans	✓*†	✓*†	✓*†	✓*†	✓*†	✓*†	✓*†	✓*†

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

2.1 Chest Radiographs (CXRs)

Chest radiographs (CXRs) will be performed in accordance with the standard practices of the participating sites. In general, participating sites are asked to obtain posteroanterior (PA) and lateral views for all participants that have been randomized to an intervention phase arm that requires CXRs to be obtained.

2.2 Chest Computed Tomography (CT) Scans

Chest computed tomography scans (CT) will be performed in accordance with the standard practices of the participating sites. In general, participating sites are asked to obtain posteroanterior (PA) and lateral views and contrast is not required.

2.3 Intervention Phase Thoracic Imaging Protocol Deviations

2.3.1 Unscheduled Thoracic Imaging

As per the study protocol, site investigators may have a participant obtain additional, unscheduled thoracic imaging any time they are concerned, even if it breaks the surveillance protocol to which the participant was assigned. Should a participant obtain unscheduled thoracic imaging during the study intervention phase (i.e., anytime during the first two years of the study), 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.

2.3.2 Improper Thoracic Imaging Modality

As per the study protocol, site investigators may have a participant obtain thoracic imaging in a modality to which the participant was not assigned at any time they are concerned, even if it breaks the surveillance protocol (i.e., obtain a chest CT scan even though the participant was allocated to CXR). Should a participant obtain a thoracic imaging modality not consistent with his / her surveillance allocation during the study intervention phase (either intentionally or accidentally), 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.

2.3.3 Missed Thoracic Imaging

Efforts should be undertaken to ensure the participant obtains the appropriate thoracic imaging in the acceptable intervention phase visit windows (**Table 2**), including having the participant to obtain his / her thoracic imaging at an outside location provided that the clinical site personnel can obtain a copy of these images. If a participant is unable to obtain thoracic imaging at any time during the study intervention phase, a **Protocol Deviation Form (Form 19)** should be completed to indicate 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.

Table 2. 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

3.0 Post-Intervention Phase Thoracic Imaging

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, thoracic imaging may be obtained as part of the standard of care post-operative follow-up appointments. See **Table 3** below for the thoracic imaging schedule at each of the post-intervention phase visits. It is possible for a participant to obtain his / her thoracic imaging at an outside location provided that the clinical site personnel can obtain a copy of these images and the appropriate clinical assessment is still conducted during a post-operative surveillance visit (see **Study Follow-Up Guidelines** in the Study Resource Binder). Details of the participant's thoracic imaging will be recorded on the **Post-Intervention Phase Surveillance Visit Form (Form 9)**. For guidelines on the completion of this CRF, please refer to **Case Report Form Completion Guidelines** in the Study Resource Binder

Table 3. Post-Intervention Phase Thoracic Imaging Schedule

Data Collection	***Post-Intervention Phase Visits***					
	30M Visit	**36M Visit**	**42M Visit**	**48M Visit**	**54M Visit**	**60M Visit**
Imaging						
Thoracic Imaging (Chest Radiograph OR Chest CT Scan)	✓	✓	✓	✓	✓	✓

✓ Required ✦ As Needed

Whenever possible, the thoracic imaging modality to which a participant was originally allocated in the intervention phase (CXR OR chest CT scan) should be obtained at least every six months according to the acceptable post-intervention phase visit windows (**Table 4**). However, if the site investigator determines the participant requires thoracic imaging to which the participant was not originally allocated (including an imaging modality not consistent with any of the SAFETY Trial imaging modalities [i.e., positron emission tomography [PET] scans or magnetic resonance imaging [MRI]) at any of the post-intervention phase surveillance visits, this thoracic imaging may be utilized without constituting a protocol deviation. Furthermore, as per the study protocol, site investigators may have a participant obtain additional, unscheduled thoracic imaging any time they are concerned, without constituting a protocol deviation. Details of these events will be recorded on the **Post-Intervention Phase Surveillance Visit Form (Form 9)**.

Table 4. 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

4.0 Frequently Asked Questions

This section provides clarification and guidance on the study imaging procedures. Please contact the Methods Center if you have any questions about the study imaging of a particular participant in the trial.

4.1 Are there certain standards that must be followed when obtaining thoracic imaging?

Please perform all CXRs and CT scans in accordance with the standard practices of the participating sites.

4.2 What if the participant did not obtain the required thoracic imaging prior to the surveillance clinic visit?

If the participant does not receive the required thoracic imaging prior to the surveillance clinic visit, please make every effort to have the participant obtain the required thoracic imaging within the acceptable intervention phase or post-intervention phase visit windows.

If the acceptable intervention phase visit window passes and the participant has not obtained the required thoracic imaging in the intervention phase visit, please record this on a **Protocol Deviation Form (Form 19)**. If the acceptable post-intervention phase visit window passes and the participant has not obtained the required thoracic imaging within the post-intervention phase visit, please record details of this event on the **Post-Intervention Phase Surveillance Visit Form (Form 9)**. A **Protocol Deviation Form (Form 19)** is NOT required.

4.3 What if the participant accidently received a whole-body PET scan?

If a whole-body PET scan was performed during the study intervention phase, please complete a **Protocol Deviation Form (Form 19)**. If a whole-body PET scan was performed during the study post-intervention phase, please record details of this scan on the **Post-Intervention Phase Surveillance Visit Form (Form 9)**. A **Protocol Deviation Form (Form 19)** is NOT required.