



SAFETY

Surveillance After Extremity Tumor Surgery

Tumor Grading and Staging Guidelines

Version 1.0

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Document History

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

1.0 Introduction

The purpose of this document is to provide guidance on how to properly report the tumor grade and stage for the **Surveillance AFter Extremity Tumor surgery (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 tumor grade and stage reporting, they should contact the Project Manager at the Methods Center via email and / or telephone.

2.0 Fédération Nationale des Centres de Lutte Contre Le Cancer (FNCLCC) Tumor Grade

The Fédération Nationale des Centres de Lutte Contre Le Cancer (FNCLCC) tumor grade is being collected for each participant in the SAFETY trial (see **Baseline Tumor Pathology Form**). This information is likely reported on the pathology report that was issued after the participant's initial surgery.

The FNCLCC grading system divides sarcomas into three distinct grades (one to three). The grade of the sarcoma helps predict how quickly the tumor will grow and spread. The grade of a sarcoma is determined by three factors:

- **Tumor Differentiation:** Cancer cells are scored from one to three for differentiation, with one being assigned when they appear much like normal cells and three being assigned when the cancerous cells look very abnormal and unlike normal cells. Certain sarcoma types are automatically assigned a higher score.
- **Mitotic Count:** Cancer cells are scored from one to three for mitotic count (the number of cancer cells seen dividing under the microscope), with a lower score meaning fewer cells were seen dividing.
- **Tumor Necrosis:** Cancer cells are scored from zero to two for tumor necrosis (the amount of the tumor that is made up of dying tissue), with a lower score meaning less of the tumor is made up of dying tissue.

Table 1. FNCLCC Histologic Grading System

Score	Description / Example
<i>Tumor Differentiation</i>	
1	Sarcoma closely resembles normal adult mesenchymal tissue (e.g., well differentiated liposarcoma)
2	Sarcomas for which histologic typing is certain (e.g. myxofibrosarcoma)
3	Embryonal and undifferentiated sarcomas, sarcomas of doubtful type and synovial sarcomas
<i>Mitotic Count</i>	
1	0 – 9 mitoses per 10 high-power fields (HPF) [†]
2	10 – 19 mitoses per 10 HPF
3	≥ 20 mitoses per 10 HPF
<i>Tumor Necrosis</i>	
0	No necrosis
1	< 50% tumor necrosis
2	≥ 50% tumor necrosis

†A HPF measures 0.1734 mm².

Once each factor is scored for a tumor, the factor scores are added to determine the grade of the tumor (see **Table 2** below).

Table 2. FNCLCC Tumor Grades

Grade	Description
Grade One	Total score of 2 or 3
Grade Two	Total score of 4 or 5
Grade Three	Total score of 6, 7 or 8

Adapted from:

Trojani M, Contesso G, Coindre JM, et al. Soft-tissue sarcomas of adults; study of pathological prognosis variables and definition of a histopathological grading system. *Int J Cancer*. 1984; 33: 37 – 42.

3.0 American Joint Committee on Cancer (AJCC) Tumor Staging

Similarly, the American Joint Committee on Cancer (AJCC) tumor stage is also being collected for each participant in the SAFETY trial (see **Baseline Tumor Pathology Form**). This information is likely also reported on the pathology report that was issued after the participant’s initial surgery.

The AJCC staging system divides extremity sarcomas into four stages (I to IV). The grade of the sarcoma helps predict how quickly the tumor will grow and spread. The stage of a sarcoma is determined by four factors:

- **Tumor:** The extent of the tumor. How large is the cancer?
- **Nodes:** The spread to nearby lymph nodes. Has the cancer spread to nearby lymph nodes?
- **Metastasis:** The spread (metastasis) to distant sites. Has the cancer spread to distant organs such as the lungs?
- **Grade:** The grade of the cancer. How much do the sarcoma cells look like normal cells?

Table 3. AJCC Staging System

Score	Description
<i>Tumor</i>	
T1	The tumor is five centimeters or smaller.
T2	The tumor is five centimeters but not more than ten centimeters.
T3	The tumor is ten centimeters but not more than fifteen centimeters.
T4	The tumor is larger than fifteen centimeters.
<i>Nodes</i>	
N0	The cancer has not spread to nearby lymph nodes.
N1	The cancer has spread to nearby lymph nodes.
<i>Metastasis</i>	
M0	The cancer has not spread to distant sites.
M1	The cancer has spread to distant sites (such as the lungs).
<i>Grade</i>	

G1	The cancer is considered a Grade One tumor.
G2	The cancer is considered a Grade Two tumor.
G3	The cancer is considered a Grade Three tumor.

Once each factor is scored for a tumor, the factor scores are used to determine the stage of the tumor (see **Table 4** below).

Table 4. AJCC Tumor Stages

<i>When T is ...</i>	<i>And N is ...</i>	<i>And M is ...</i>	<i>And G is ...</i>	<i>Then the stage is ...</i>
T1	N0	M0	G1, GX	IA
T2, T3, T4	N0	M0	G1, GX	IB
T1	N0	M0	G2, G3	II
T2	N0	M0	G2, G3	IIIA
T3, T4	N0	M0	G2, G3	IIIB
Any T	N1	M0	Any G	IV
Any T	Any N	M1	Any G	IV

Adapted from:

Amin MB, Greene FL, Edge SB, et al. AJCC Cancer Staging Manual. 8th Ed. Springer International Publishing; 2017.