Surveillance AFter Extremity Tumor surgerY International Randomized Controlled Trial

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Does the frequency and mode of surveillance affect patient survival following extremity STS surgery?

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Musculoskeletal and connective tissue neoplasms
Study type	Interventional

Summary

ID

NL-OMON52065

Source
ToetsingOnline

Brief title
SAFETY

Condition

- Musculoskeletal and connective tissue neoplasms
- Soft tissue neoplasms malignant and unspecified

Synonym
soft tissue sarcoma - soft tissue cancer

Research involving
Human

Sponsors and support

Primary sponsor: Hamilton Academic Health Sciences Organization
Source(s) of monetary or material Support: Hamilton Academic Health Sciences Organization

Intervention

Keyword: Lung Metastases, Soft Tissue Sarcoma

Outcome measures

Primary outcome

The primary outcome for the definitive trial will be overall five-year survival. The primary outcome measure will be death from any cause.

Secondary outcome

Patient Anxiety Outcome Measure: The validated Patient-Reported Outcomes Measurement Information System (PROMIS)® Cancer-Anxiety questionnaire will be used to assess patient anxiety. This questionnaire will be administered at the baseline visit, as well as the 6-month, 12-month, 18-month and 24-month intervention phase and 36-month, 48-month and 60-month post-intervention phase visits.

Patient Overall Satisfaction Outcome Measure: The validated PROMIS® Satisfaction with Social Roles and Activities questionnaire will be used to assess patient overall satisfaction. This questionnaire will be administered at the baseline visit, as well as the 6-month, 12-month, 18-month and 24-month intervention phase and 36-month, 48-month and 60-month post-intervention phase visits.

Quality of Life Outcome Measure: The validated EuroQol-5 Dimension (EQ-5D) will be used to assess patient quality of life. This questionnaire will be administered at the baseline visit, as well as the 6-month, 12-month, 18-month

and 24-month intervention phase and 36-month, 48-month and 60-month post-intervention phase visits.

Local Recurrence-Free Survival (LRFS) Outcome Measure: LRFS will be defined as the length of time from the time of randomization that the participant survives with no detection of recurrent disease at the initial tumor site or operative field. Local disease recurrence and the modality in which it was identified (i.e. physical exam, MRI, ultrasound) will be documented on participant case report forms (CRFs).

Metastasis-Free Survival (MFS) Outcome Measure: MFS will be defined as the length of time from the time of randomization that the participant survives with no detection of systemic disease recurrence at any anatomic location. Systemic disease recurrence and the modality in which it was identified (CXR, CT, PET scan, bone scan) will be documented on participant CRFs.

Treatment-Related Complications Outcome Measures: Treatment-related complications will include both chemotherapy-related complications, such as febrile neutropenia, fungal infections or sepsis, and thoracotomy-related complications, such as pneumothorax or surgical site infections. All treatment-related complications will be documented on participant CRFs.

Net Healthcare Costs Outcome Measures: We will perform an incremental cost analysis of net costs of surveillance and costs incurred from metastasis

treatment and metastasis treatment-related complications. Data will be documented on participant CRFs at each outpatient visit and hospital admission. The direct costs will include physician billing for clinic visits, per unit cost of CXR and CT scans, systemic therapy costs, hospital admission costs related to systemic therapy complications, thoracotomy costs and hospital admission costs for complications related to thoracic surgical intervention. Unit costs for all resources used by trial participants will be obtained from regional statistics and from clinical sites participating in the trial. These unit costs will be combined with the resource volumes to obtain a net cost per participant over their time in the trial.

Study description

Background summary

Following treatment for a soft tissue sarcoma (STS) that is not metastatic at presentation, the risk for local and systemic disease recurrence necessitates careful post-operative surveillance. Between 40 and 50% of all sarcoma patients will develop a local or distant recurrence; however, the risk of recurrence is greatest in the first few years, with 68% occurring by two years and 90% by five years. Metastasis to the lung is the most frequent single location of disease recurrence in sarcoma patients, occurring in the majority of patients with metastases. Therefore, routine follow-up after completing sarcoma treatment is standard practice, and generally entails regular visits to sarcoma outpatient clinics in the first five years after surgery. These visits typically include a clinical history, physical examination and imaging of the lungs (chest radiograph [CXR], or computed tomography [CT] scan of the lungs). Earlier detection of less advanced and resectable disease recurrence may prolong patient survival. However, once advanced metastases are detected, the median length of survival is 12 to 15 months and systemic chemotherapy has little impact on overall survival. Based on retrospective cohort data, the five-year survival following the diagnosis of metastases is 15%. It is not clear if this 15% survival is achieved by earlier detection as no studies have yet to confirm the survival benefit of intense surveillance in STS. Regular, intensive surveillance is more likely to identify recurrent disease

earlier than would less intensive surveillance. However, the adverse effects of intensive surveillance practices are also noteworthy. The costs that healthcare systems incur as a result of sarcoma surveillance are substantial. Furthermore, intensive surveillance can threaten the financial security of patients, due in part to the direct (including travel, accommodation, personal care and homemaking) and indirect costs (including lost wages for patients and their caregivers) incurred as a result of follow-up appointments. As a result, patients* health and quality of life can be dramatically impacted

Study objective

Does the frequency and mode of surveillance affect patient survival following extremity STS surgery?

Study design

The SAFETY trial is a multi-center 2X2 factorial RCT of participants with extremity STS who present without metastases and who require surgical management and post-operative surveillance for local and systemic disease recurrence with a total follow-up of 5 year.

Intervention

Participants will be randomized to one of four treatment / surveillance groups:
1) Clinical assessment and CXR every three months for two years;
2) Clinical assessment and CXR every six months for two years;
3) Clinical assessment and Chest CT every three months for two years; or
4) Clinical assessment and Chest CT every six months for two years.

Study burden and risks

The burden and risks associated with participation differ little from standard care.

Depeding on randomisation patients surveillance will be 3 monthly for the fosrt 2 years or 6 mornthly for the forst 2 years. Depending on randomisatien patient will have a chest X-ray of CT scan of the chest. This implies radiation, however, these additional exams are also embedded in the current standard of care.

At baseline and at follow-up questionnaires will be completed. Some questions are of personal nature and can be perceived as uncomfortable.

Participation in this trial does not change the risk of recurrence of sarcoma or development of distant metastatis.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Patients who satisfy all of the eligibility criteria outlined below are to be included in the SAFETY trial:
1) The patient is 18 years of age or older;
2) The patient has been diagnosed with a primary extremity grade II or III STS;
3) The patient has undergone surgical excision of the tumor with curative intent and with no evidence of gross residual disease based on the pathology report;
4) The patient has completed all planned neoadjuvant or adjuvant radiation and / or chemotherapy, if applicable;
5) The tumor size is greater than or equal to five centimeters according to the pathology report or based on the pre-treatment MRI if neoadjuvant radiation and

/ or chemotherapy are given

Exclusion criteria

Patients who meet any of the following criteria are not to be included in the SAFETY trial:
1) The patient has metastases at initial presentation based on the radiology report of the initial thoracic imaging;
2) The patient has recently undergone surgical excision of a local recurrence;
3) The patient has been diagnosed with one of the special sub-types, myxoid / round cell liposarcoma or extra-skeletal Ewing*s sarcoma;
4) The patient has been previously diagnosed with a genetic syndrome with an elevated risk of malignancy, such as Li-Freumeni Syndrome*;
5) The patient has been previously diagnosed with a co-morbid condition that has a life expectancy of less than one year;
6) 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);
7) Likely problems, in the judgment of the investigator, with the patient maintaining follow-up (with the specific reasoning requiring approval of the Methods Center);
8) The patient is currently enrolled in a study that does not permit co-enrolment

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	03-11-2021

Enrollment:	50
Type:	Actual

Ethics review

Approved WMO Date:	25-08-2021
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	11-03-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
ClinicalTrials.gov	NCT03944798
CCMO	NL76116.058.20