

The Surveillance After Extremity Tumor Surgery (SAFETY) International Multi-Center Randomized Controlled Trial

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Significance & Hypothesis/Techniques

Optimal pulmonary surveillance following surgery for extremity soft-tissue sarcoma remains uncertain, particularly with respect to imaging modality and surveillance frequency. Because surveillance strategies may affect survival, treatment burden, serious adverse events, and patient anxiety, high-level evidence is needed to inform follow-up practice. SAFETY was designed to determine whether the frequency and mode of pulmonary surveillance influence patient-important outcomes after extremity soft-tissue sarcoma surgery.

Innovation

SAFETY is an international multicenter randomized controlled trial evaluating both surveillance modality and surveillance frequency within a single trial design. The study uses a hierarchical composite primary outcome incorporating overall survival, serious adverse events, and patient-reported anxiety, enabling assessment of oncologic outcomes alongside the patient experience of surveillance.

Approach

Patients were randomized to 1 of 4 surveillance strategies during the first 2 years of follow-up: chest radiography every 3 months, computed tomography of the chest every 3 months, chest radiography every 6 months, or computed tomography of the chest every 6 months. The target sample size was 310 patients. All participants will be followed for a minimum of 3 years and up to 5 years after randomization.

Results

Enrollment was completed in October 2024 with 310 randomizations across 35 clinical sites in 14 countries. Within the pilot cohort, 14% of patients died within the first 2 years after randomization. Many patients now have 4- and 5-year follow-up. The independent data and safety monitoring board has recommended that the trial continue as designed. Study closeout is planned for the end of 2027.

Discussion & Impact

SAFETY represents a large global collaborative effort in orthopaedic oncology and demonstrates the feasibility of completing an international randomized surveillance trial in sarcoma. As follow-up matures, the study will provide evidence to guide shared decision-making regarding post-treatment pulmonary surveillance in high-risk extremity soft-tissue sarcoma, allowing surveillance strategies to be aligned more closely with both clinical outcomes and patient preferences.