Hypofractionated, 3-week, preoperative radiotherapy for patients with softæ tissue sarcomas (HYPORT-STS): a single-centre, open-label, single-arm, phase 2 trial

B Ashleigh Guadagnolo, Roland L Bassett, Devarati Mitra, Ahsan Farooqi, Caroline Hempel, Courtney Dorber, Tiara Willis, Wei-Lien Wang, Ravin Ratan, Neeta Somaiah, Robert S Benjamin, Keila E Torres, Kelly K Hunt, Christopher P Scally, Emily Z Keung, Robert L Satcher, Justin E Bird, Patrick P Lin, Bryan S Moon, Valerae O Lewis, Christina L Roland, Andrew J Bishop

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Clinical Trial

BACKGROUND

The standard preoperative radiotherapy regimen of 50 Gy delivered in 25 fractions for 5 weeks for soft tissue sarcomas results in excellent local control, with major wound complications occurring in approximately 35% of patients. We aimed to investigate the safety of a moderately hypofractionated, shorter regimen of radiotherapy, which could be more convenient for patients.

METHODS

This single-centre, open-label, single-arm, phase 2 trial (HYPORT-STS) was done at a single tertiary cancer care centre (MD Anderson Cancer Center, Houston, TX, USA). We administered preoperative radiotherapy to a dose of 42·75 Gy in 15 fractions of 2·85 Gy/day for 3 weeks (five fractions per week) to adults (aged ≥18 years) with non-metastatic soft tissue sarcomas of the extremities or superficial trunk and an Eastern Cooperative Oncology Group performance status of 0-3. The primary endpoint was a major wound complication occurring within 120 days of surgery. Major wound complications were defined as those requiring a secondary operation, or operations, under general or regional anaesthesia for wound treatment; readmission to the hospital for wound care; invasive procedures for wound care; deep wound packing to an area of wound measuring at least 2 cm in length; prolonged dressing changes; repeat surgery for revision of a split thickness skin graft; or wet dressings for longer than 4 weeks. We analysed our primary outcome and safety in all patients who enrolled. We monitored safety using a Bayesian, one-arm, time-to-event stopping rule simulator comparing the rate of major wound complications at 120 days post-surgery among study participants with the historical rate of 35%. This trial is registered with ClinicalTrials.gov, NCT03819985, recruitment is complete, and follow-up continues.

FINDINGS

Between Dec 18, 2018, and Jan 6, 2021, we assessed 157 patients for eligibility, of whom 120 were enrolled and received hypofractionated preoperative radiotherapy. At no time did the stopping rule computation indicate that the trial should be stopped early for lack of safety. Median postoperative follow-up was 24 months (IQR 17-30). Of 120 patients, 37 (31%, 95% CI 24-40) developed a major wound complication at a median time of 37 days (IQR 25-59) after surgery. No patient had acute radiation toxicity (during radiotherapy or within 4 weeks of the radiotherapy end date) of grade 3 or worse (Common Terminology Criteria for Adverse Events [CTCAE] version 4.0) or an on-treatment serious adverse event. Four (3%) of 115 patients had late radiation toxicity (≥6 months post-surgery) of at least grade 3 (CTCAE or Radiation Therapy Oncology Group/European Organisation for Research and Treatment of Cancer Late Radiation Morbidity Scoring Scheme): femur fractures (n=2), lymphoedema (n=1), and skin ulceration (n=1). There were no treatment-related deaths.

INTERPRETATION

Moderately hypofractionated preoperative radiotherapy delivered to patients with soft tissue sarcomas was safe and could therefore be a more convenient alternative to conventionally fractionated radiotherapy. Patients can be counselled about these results and potentially offered this regimen, particularly if it facilitates care at a sarcoma specialty centre. Results on long-term oncological, late toxicity, and functional outcomes are awaited.