IMRIS TRIAL SUMMARY

Title:	A phase II study of intensity modulated radiotherapy (IMRT) in primary bone and soft tissue sarcoma
Short Title/acronym:	IMRiS
Sponsor name & reference:	University College London (UCL/13/0376)
Funder name:	Cancer Research UK (C2921/A17558)
Design:	**A prospective multicentre phase II trial with three separately analysed cohorts:** Cohort 1: Limb/limb girdle soft tissue sarcoma (STS) receiving (neo)-adjuvant radiotherapy (RT) Cohort 2: Patients with Ewing's sarcoma of the spine/pelvis receiving definitive radical or (neo)-adjuvant RT Cohort 3: Patients with non-Ewing's primary bone sarcomas of the spine/pelvis receiving definitive radical or adjuvant RT
Overall aim:	To assess the feasibility, efficacy and toxicity of IMRT in three different cohorts of patients with bone and soft tissue sarcoma and to demonstrate whether IMRT can improve on current clinical outcomes.
Primary endpoint:	Cohort 1: The rate of grade 2 or more late soft tissue fibrosis at 2 years following RT. Cohorts 2 and 3: The proportion of patients where ≥95% of the recommended optimal RT dose can be achieved with IMRT.
Secondary endpoints:	Cohort 1: Acute and late RT toxicity; patient reported limb function and quality of life; rate and severity of wound complications within 120 days of surgery; time to local tumour recurrence; disease free and overall survival. Cohorts 2 and 3: Acute and late RT toxicity; response by RECIST 1.1 (for definitive radical RT); patient reported quality of life; time to local recurrence (for adjuvant RT); time to local disease progression (for definitive radical RT); disease-free survival; overall survival.
Target accrual:	143 patients over 2 years:

	Cohort 1: 110 patients; Cohort 2: 21 patients; Cohort 3: 12 patients
Inclusion & exclusion criteria:	Inclusion criteria: • Histological proven soft tissue sarcoma of the upper or lower limb or limb girdle, *or* • Ewing's sarcoma of bone arising in the pelvis or spine, *or* • High grade primary bone sarcoma (non-Ewing's) or chordoma arising in the pelvis or spine • Patients requiring (neo)adjuvant or definitive radical radiotherapy • WHO performance status 0-2 • Patients aged ≥ 16 years Exclusion criteria: • Previous radiotherapy to the same site • Patient with bone sarcomas eligible for proton beam radiotherapy via the UK Proton Panel • Paediatric type alveolar or embryonal rhabdomyosarcomas • Pregnancy • Patients with concurrent or previous malignancy that could compromise assessment of primary and secondary endpoints of the trial
Treatment summary:	Radiotherapy will be delivered with fixed beam IMRT, arc IMRT techniques, or tomotherapy. Dose schedules: **Cohort 1** Pre-operative RT – 50 Gy in 25 daily fractions over 5 weeks; Post-operative RT – 60 Gy in 30 daily fractions to the high dose planning target volume (PTV) and 52.2 Gy in 30 daily fractions to the low dose PTV treated concurrently over 6 weeks; Post-operative RT (positive resection margins) – 66 Gy in 33 daily fractions to the high dose PTV, and 53.46Gy in 33 fractions to the low dose PTV treated concurrently over 6 ½ weeks **Cohort 2** Pre-operative RT – 50.4 Gy in 28 daily fractions over 5½ weeks; Post-operative RT - 54 Gy in 30 daily fractions over 6 weeks; Primary RT - 54 Gy in 30 daily fractions over 6 weeks **Cohort 3**

	Primary RT – 70 Gy in 35 daily fractions over 7 week; Post-operative RT (non-chordoma) – primary bone sarcoma 60 Gy in 30 daily fractions over 6 weeks; Post-operative RT (chordoma) – 70 Gy in 35 daily fractions over 7 weeks
Anticipated duration of recruitment:	2 years
Duration of patient follow up:	A maximum of three years after registration
Definition of end of trial:	3 years after registration of the final patient or death of all patients, whichever is sooner

Coordinating Centre:

For general queries, supply of trial documentation and central data management	**IMRiS Trial Coordinator** Cancer Research UK & UCL Cancer Trials Centre 90 Tottenham Court Road, London W1T 4TJ Tel: +44 (0) 20 7679 9281 Fax: +44 (0) 20 7679 9871 Email: ctc.imris@ucl.ac.uk

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