ICONIC Protocol Version History Log

Name of Trial: ICONIC: Improving outcomes through Collaboration in OsteosarComa

Name of Chief Investigator: Dr Sandra Strauss

Vn	Date	Main changes	Amndt No.	REC/HRA Approval Date	Date(s) of distribution to sites & collaborators
1	07/03/2019	n/a (initial)	n/a	10/05/2019	Dependent on distribution of local information pack.
2	23/01/2020	• References to *snap frozen* changed to *fresh frozen according to local policy*. • Exclusion criteria changed to registration within **4 months** of diagnosis • Early Diagnosis (ED) questionnaire should be completed within 3m of registration. • Parent completes ED Questionnaire for patients < 13. • Baseline blood can be collected if pt has chemotherapy before registration • RNOH tissue samples are returned at end of study • Tissue samples collected at relapse/resection of local recurrence or metastases if **not** done as part of SOC. This is optional for patient.	2	25/03/2020	08/04/2020 21/09/2020 DocuSigned copy.

3	25/06/2021	• Appendix 1, abbreviations, now moved to start of protocol. Now remote consent
		• Appendix 2, Schedules reviewed and updated.
		• Trial summary: SAM taken at registration
		• 5.2: Additional information for patients lacking capacity to consent added
		• 5.3: Remote consent added
		• 9 and 10: Clarification that whole blood samples taken at site
		  • Removal of reference to at least 50 patients for CTC bloods
		  • Confirmation that bloods should be taken at clinic follow up, no more than 6 monthly
		  • Clarification for procedure for submission of CTC blood samples
		  • Clarification that ctDNA samples are to be taken for all consenting patients
		• 14: instructions on remote monitoring updated
		• 15 clarification on withdrawal of patients.
			5	REC: 28/07/21
				HRA: 31/07/21
					03/08/21 unsigned in error (incident reported: see filenote)
					
					DocuSigned copy. 09/08/2021

4	23/09/2022	• **1.1:** Stage 2 main objectives: • 'To enrol at least 160 patients' changed to 'to enrol 160 – 220 patients' • Target accrual stage 2: • Change of total number of patients from ' minimum 160 patients recruited over 3 years' to '160 – 220 patients recruited over 3 years 3 months' • Duration of recruitment: • Changed from '3 years' to '3 years 3 months' • **17.1:** 'Since recruitment is expected to last for 3 years in total (Stage 1 + Stage 2), the total expected sample size will be at least 160 patients'	7	REC: 23/09/22 HRA: 23/09/22	Date of implementation: 31/10/2022 Date of release to sites: 23/09/2022

Vn	Date	Main changes	Amndt No.	REC/HRA Approval Date	Date(s) of distribution to sites & collaborators
		• changed to: • 'Since recruitment is expected to last for 3 years 3 months in total (Stage 1 + Stage 2), the total expected sample size will be 160 - 220 patients'			

5	17/03/2023	• References to fresh frozen changed to fresh/frozen to accommodate collection for UCLH/RNOH IO samples.
		• **1.1:**
		  • addition of new stage 2 objectives.
		  • End of study definition changed to 2 years after recruitment of last patient
		  • Target no. of patients changes to at least 350
		  • Duration of FUP changed to at least 56 months.
		• **1.2:** addition of study flowchart
		• **2.2.4:** Addition of section on immune oncology research.
		• **4.1.2:** Deletion of requirement for GCP training as ICONIC is a non-CTIMP observational study.
		• **5.2:** Addition of This Clause is not to be applied at any Scottish or Northern Irish ICONIC site. To start of section.
		• **6.2:** Addition of Patients who do not consent to completion of PROs but are willing to donate blood and/or tissue samples are eligible for the Study.
		• **9:** Addition of collection of PMBC samples for 20 UCLH patients throughout section 9.
		• **9:** Addition of If the baseline ctDNA sample was missed for any reason, please continue with the on treatment, end of treatment and follow up samples throughout section.
		• **9.2.2:** Addition of The SAM booklet can be completed over the phone as well as by post or in person
		• **10.2:** Addition of We anticipate collection of fresh frozen tumour specimens, where possible, on request. At the end of the Study all routine fresh frozen tumour specimens will be returned to site.
		• **14.2:** Addition of section on remote monitoring
		• **14.3.3**: The UCL CTC Director is named as custodian of data generated in the study.
			11	REC: 20/06/2023
				HRA: 20/06/2023
					Date of implementation: 06/07/2023
					Date of release to sites: 20/03/2023
					Docusigned copy to sites on receipt of FO: 22/06/2023