ICONIC

IMPROVING OUTCOMES THROUGH COLLABORATION IN OSTEOSARCOMA

A BONE CANCER RESEARCH TRUST FUNDED PROJECT

Professor Sandra Strauss PhD FRCP – Chief Investigator,

Professor of Medical and TYA Oncology,

UCL Cancer Institute, London

On behalf of TMG and Co-investigators: Bernadette Brennan, Craig Gerrand, Kenneth Rankin, Robin Young, Michael Parry, Jonathan Stevenson, Adrienne Flanagan, Jenny Sheriff, Dominique Heymann, Rachel Taylor, Lorna Fern, Kevin Litchfield, Matthew Pugh, Saurabh Singh, Emine Hatipoglu; **CR UK & UCL CTC**: Rubina Begum Senior Project Manager, Krystyna Reczko Trial Manager, Molly Richardson, Data Manager, **William Wilson** Statistician **Patient Advocate: Filipa Vance**

DECLARATION OF INTERESTS

GSK, Inhibrx, TessioBio, Bayer – Advisory Board

Awen Oncology- Medical advisor

Boehringer Ingelheim – Educational speaker

Ipsen- Independent Data monitoring committee

NCRI National Cancer Research Institute

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CANCER RESEARCH UK | CANCER TRIALS CENTRE | UCL

Developed through UK NCRI Sarcoma Clinical Studies Group (Bone subgroup)

- to accelerate development of new treatments and ways to improve outcome for osteosarcoma by
- forming a **multi-disciplinary collaboration** to **address clinical and biological questions**
- recruiting **newly-diagnosed patients** of **all ages across the UK to build a comprehensive clinical dataset** and **tissue resource, inclusive of data on patient experience**

Primary objective: to recruit 330-350 patients across UK

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WP1: Clinical objectives

- Patterns and processes of care
- Variation in management across age and primary sites
- Local therapy -surgical decision-making

WP 2: Imaging objectives

WP3: Biology –biomarkers and immunology

WP4: Patient experience

- Diagnostic journeys
- Quality of Life and functional outcomes


Paed onc


TYA/ / adult


Med onc


surgeons


Pathology/ biology Radiology


Pt experience, QoL


Patient advocate

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National Cancer Research Institute

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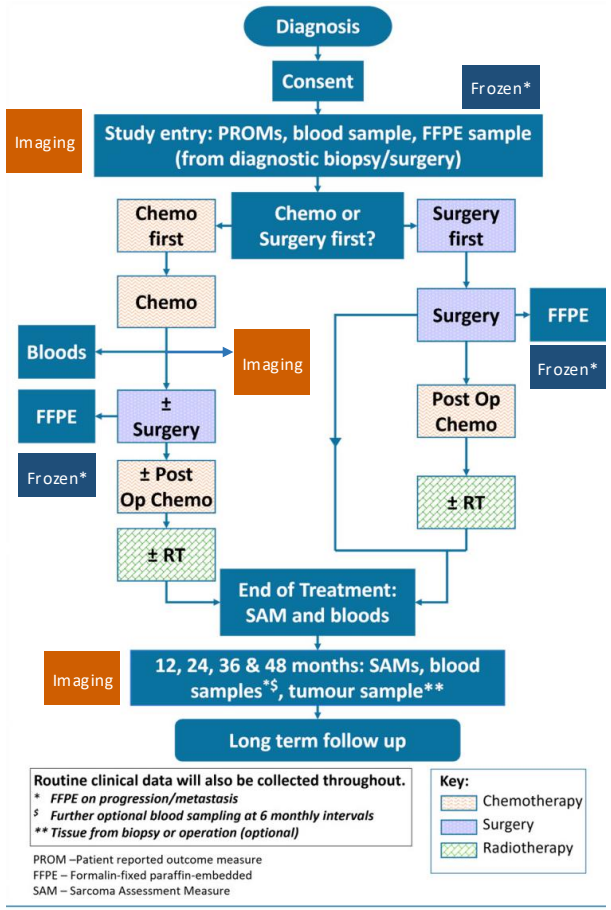
Study Design



All patients consented for use of data, imaging and samples for research in UK and abroad

National Cancer Research Institute

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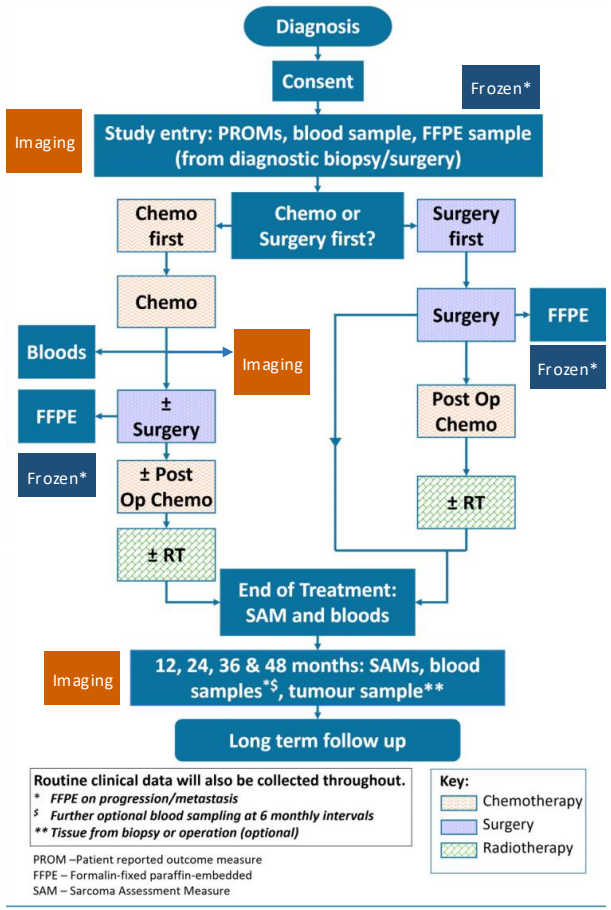

Opened Nov 2019 – funded for up to 4 years two stages

⬇

2021 – completed Stage 1: feasibility

cancers MDPI

Article

A Prospective Observational Cohort Study for Newly Diagnosed Osteosarcoma Patients in the UK: ICONIC Study Initial Results

Alexa Childs [1], Craig Gerrand [2], Bernadette Brennan [3], Robin Young [4], Kenneth S. Rankin [5], Michael Parry [6], Jonathan Stevenson [6], Adrienne M. Flanagan [2,7], Rachel M. Taylor [1], Lorna Fern [1], Dominique Heymann [8,9], Filipa Vance [10], Jenny Sherriff [11], Saurabh Singh [12], Rubina Begum [13], Sharon L. Forsyth [13], Krystyna Reczko [13], Kate Sparksman [13], William Wilson [13] and Sandra J. Strauss [1,7,*]

Cancers **2024**, *16*, 2351. https://doi.org/10.3390/cancers16132351

Confirmed feasibility
Tissue: FFPE on all pts
Frozen: 66%, but at biopsy < 30%
(+/- 30% had WGS as part of NHS care)

Blood > 70%
Pt experience: > 60%

All patients consented for use of data, imaging and samples for research in UK and abroad

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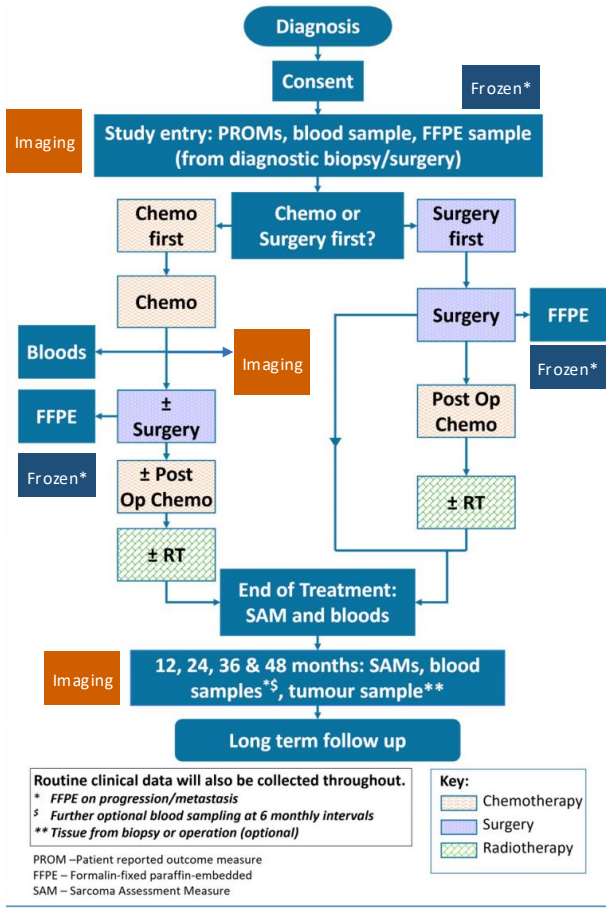

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↓

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↓

Hamilton Osteosarcoma Award- Advancing ICONIC*

Awarded June 2023- Stage 2

↓

January 2025 : Completed recruitment

cancers MDPI

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***£1M grant to support osteosarcoma research through generous donation from the Hamilton family**

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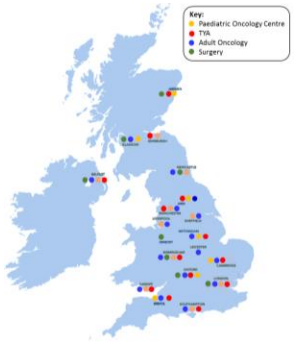
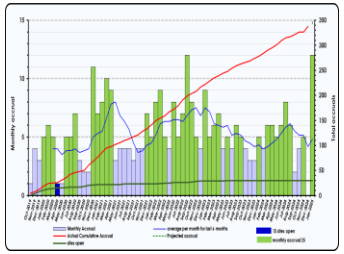
Results

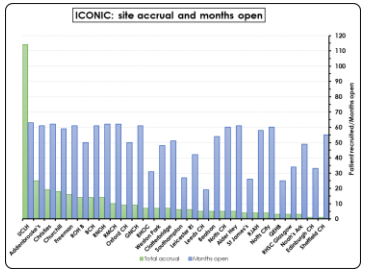
Opened 28 centres



Paediatric
TYA
Adult
surgery

Recruited 342 patients





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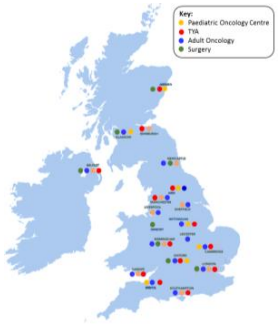
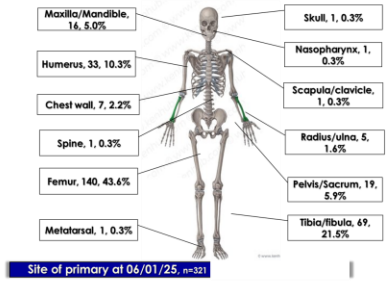


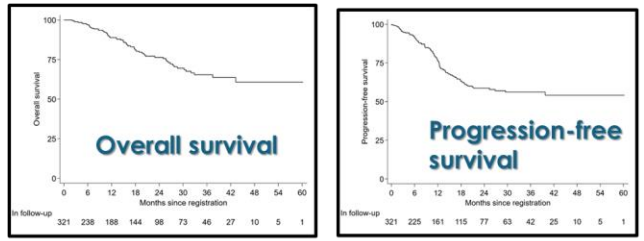
Representative patient population including rare primary sites and across ages

Age	
<16	109 (34%)
16-24	96 (30%)
25-50	83 (26%)
>50	33 (10%)

Gender	
Female	143 (44%)
Male	178 (56%)

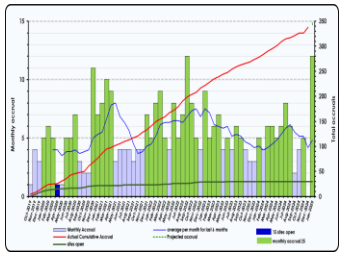
Metastatic disease	N	%
No	194	60
Indeterminate	47	15
Yes	59	18
Unknown	21	7

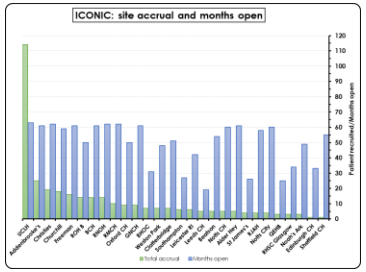




	At 12 months	At 24 months
PFS	77% (95% CI 72-82)	60% (95% CI 53-66)
OS	89% (95% CI 84-92)	77% (95% CI 70-82)

Recruited 342 patients





Insights into clinical care

Staging	
CT chest	
Yes	98 (98%)
No metastases	62/98 (63%)
Metastases confirmed	27/98 (28%)
Indeterminate	9/98 (9%)
No	2 (2%)
PET scan	
Yes	19 (19%)
No metastases	12/19 (63%)
Metastases confirmed	6/19 (32%)
Indeterminate	1/19 (5%)
No	81 (81%)
Isotope bone scan	
Yes	26 (26%)
No metastases	25/26 (96%)
Metastases confirmed	1/26 (4%)
No	74 (74%)
WB MRI for mets	
Yes	49 (49%)
No mets	43/49 (88%)
Metastases confirmed	4/49 (8%)
Indeterminate	1/49 (2%)
Report unavailable	1/49 (2%)
No	51 (51%)

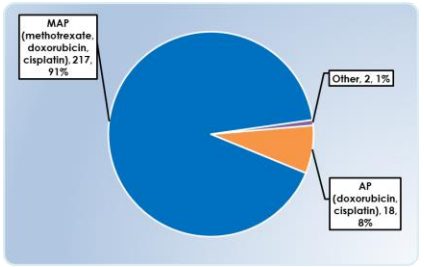
20% PET

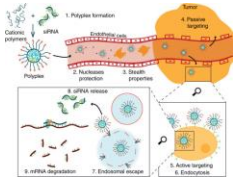
26% bone scan

51% WB MRI

Differences in skeletal staging

Median follow up time for all patients is 21 months (IQR 8.0-36.3 months)





72/109 (66%) of eligible pts received mifamurtide

Surgical studies

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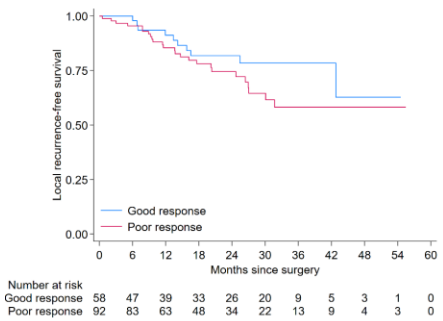
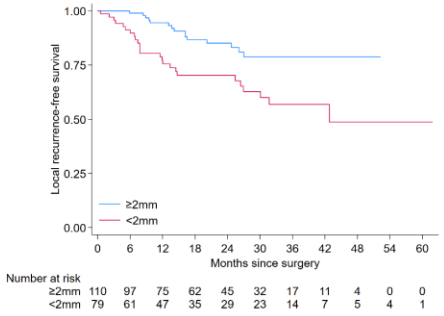
1. Impact of chemotherapy response and resection margin on local recurrence

Histological response



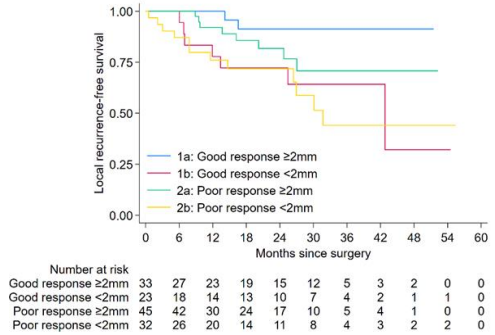
No significant difference in post-surgery local recurrence-free survival (LRFS) comparing good responders to poor responders: HR = 0.62 (95% CI 0.30-1.29), p=0.2

Narrowest resection margin



Significant difference in LRFS based on narrowest resection margin (≥2mm vs <2mm): HR = 0.38 (95% CI 0.20-0.71), p =0.003

Birmingham Classification



Patients with 1a classification significantly better than all others except 2a. No other comparisons are significant.

2. Tumour-board decision-making for challenging primary sites

- amputation
- pelvic resections

UCL CMI Centre for Medical Imaging

-imaging available through centralized imaging repository (WP2)

→ collaboration with FOSTER

FIGHT OSTEOSARCOMA THROUGH EUROPEAN RESEARCH — FOSTER

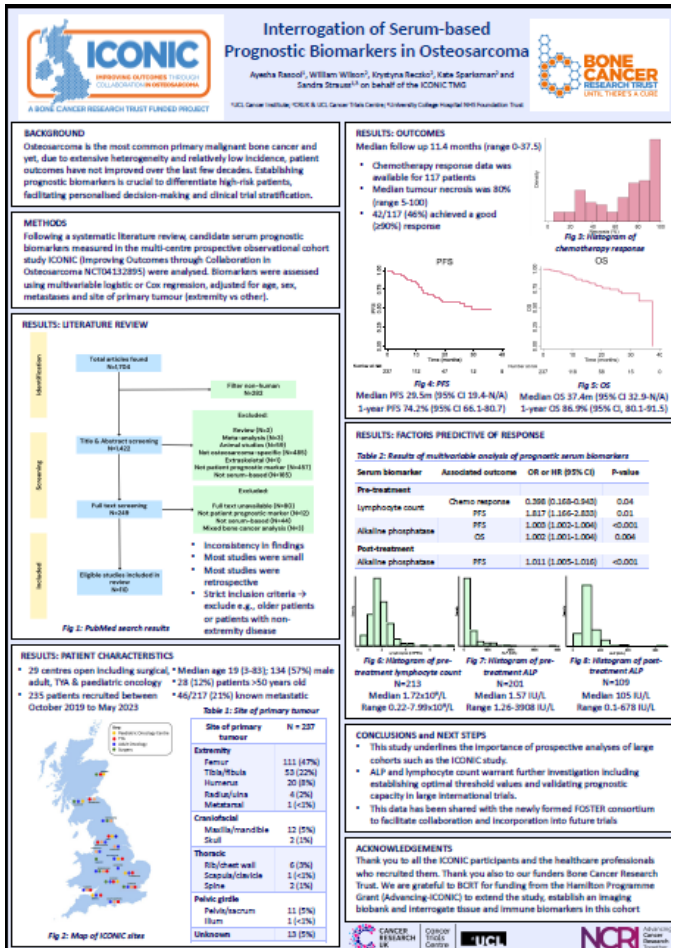
3. Contribute to EMSOS local relapse study led by Emmanuela Palmerini

SERVIZIO SANITARIO REGIONALE
EMILIA - ROMAGNA
Istituto Ortopedico Rizzoli di Bologna
Istituto di Ricovero e Cura a Carattere Scientifico

An observational study of local relapse after high grade osteosarcoma

Biology: Serum and blood biomarker studies

Serum-based Biomarkers



Multi-omic analysis of cfDNA

Plasma from 250 patients with diagnostic, pre-op, follow up and relapse (53)

Dr Pillay: UCL Neo-Sarc: Cancer Research UK, Collaboration with Andy Begg

CANCER RESEARCH UK

Funded by
Cancer Research UK

Neo-Sarc: Enhancing the clinical whole genome sequencing programme for patients with genomically complex sarcomas.

Dr Pillay, Nischalan | ORCID: 0000-0003-0579-4105 | University College London
Author profile

CANCER RESEARCH UK | CITY OF LONDON CENTRE

UCL • King's • Barts • Crick

2025 CRUK City of London Centre MBPhD studentship

Pilot studies analysis of CTC

> 50 paired samples, with 20 relapses

Kenny Rankin

CTC identification and quantification by flow cytometry

proteomic analysis of CTC – Vikky Rand,Teeside

Robin Young and Dominique Heymann

CTC identification and quantification by DEPArray

Imaging biomarker studies - Led by Saurabh Singh, UCL

National Cancer Imaging Translational Accelerator (NCITA)

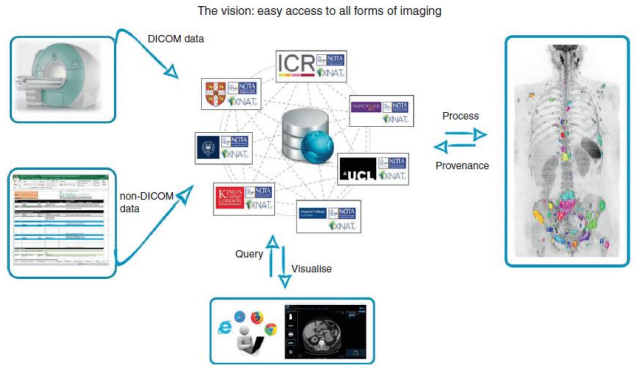
- National coordinated infrastructure for translation of imaging biomarkers for clinical use[1]. Established Imaging repositories, Standardised protocols for data integration

Aim: Establish Imaging Repository

→ SOPs developed
→ Amendment to protocol for centres – funded upfront to sites and REC already in place

→ funding a clinical fellow at UCLH commenced Jan 2025

Margaret Spittle Fellowship, Yakup Kilic



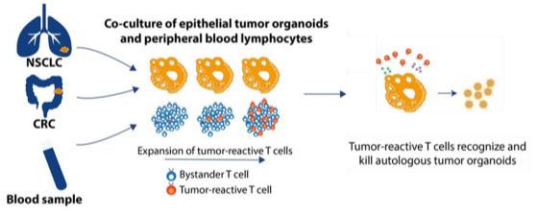
Treatment response	Pre and post chemotherapy Correlate to histological %necrosis and oncological outcomes
Imaging strategy for staging of osteosarcoma in the ICONIC trial.	Staging Imaging Indeterminate findings Number of imaging tests per patient
Radiomics-Based Prognostic Model for Osteosarcoma.	Correlation of imaging features with oncological outcomes
Preoperative Imaging Features Predicting Functional/Surgical Outcomes	Tumour size, proximity to critical structures, location correlation to margin status

1. McAteer, et al, Br J Canc, 2019

WP3-Biological objectives

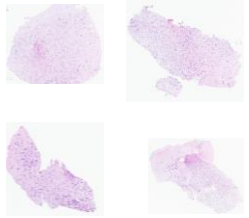
Development of patient- derived tumour models

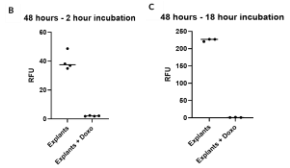
Pipeline– ICONIC tissue from surgery to UCL Primary cultures and explants



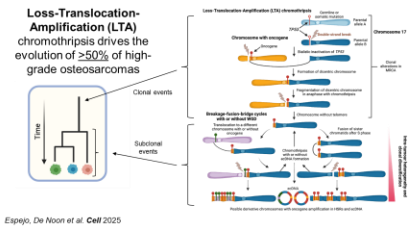
→ 2 D cultures (n=20) inc 3 lung metastases
→ Explants

SARC047

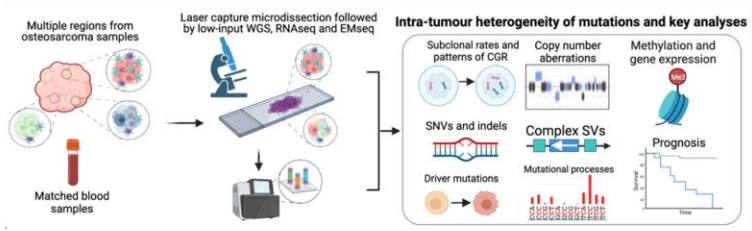




Decoding the tumour-immune cross talk in osteosarcoma



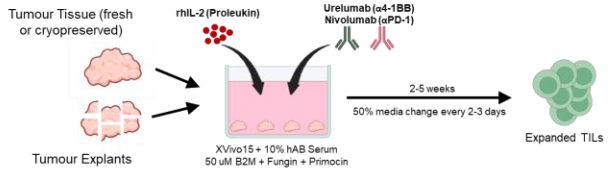
Pilot 1. Spatially resolved genomics and transcriptomics to study genomic evolution and immune evasion in osteosarcoma



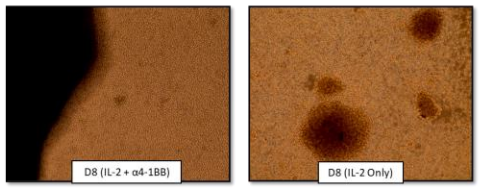
~20 patients with **matched primary and metastatic** samples

Funding OSTEOSARCOMA INSTITUTE wellcome sanger institute

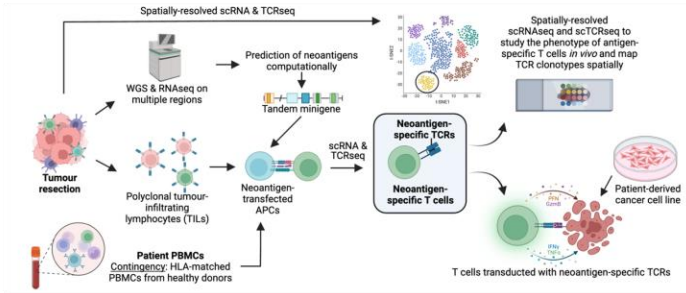
Optimized isolation of tumour infiltrating lymphocytes from osteosarcoma samples



Chris Pinder (Flanagan lab)



Isolation of TILs permits identification of which mutations are immunogenic



Funding EACR The Mark Foundation for Cancer Research Fondazione Pezcoller

WP4: Patient experience

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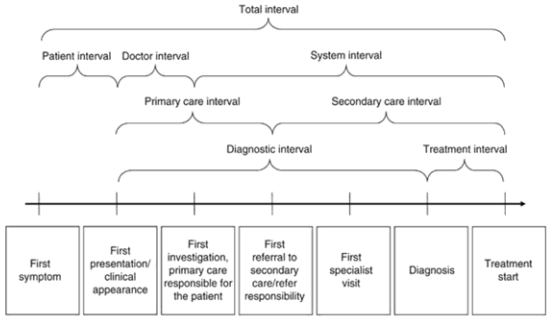
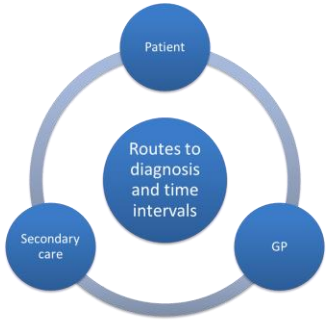
Diagnostic Journey





International Cancer Benchmarking Partnership-model

Time and routes to diagnosis

- Median No. pre-diagnostic healthcare appts 3 (1-58)
- Median time from symptoms to diagnosis 112 days (~4 months)
- 18% presented via Emergency Department (ED)
- 47% attended ED at least once

Quality of life and functional wellbeing

Patient Reported Outcomes Measures

EORTC QLQ-C30 (version 3)

TESS (Toronto Extremity Salvage Score)

Sarcoma Assessment Method (SAM)

Article

The Sarcoma Assessment Measure (SAM): Preliminary Psychometric Validation of a Novel Patient-Reported Outcome Measure

Lee Hulbert-Williams [1,*], Nicholas J. Hulbert-Williams [1], Ana Martins [2], Lesley Storey [3], Jennie Bradley [4], Hatty O'Sullivan [4], Lorna A. Fern [2], Maria Lawal [2], Rachael Windsor [5], Craig Gerrand [6], Jeremy S. Whelan [2], Lindsey Bennister [7], Mary Wells [8,9] and Rachel M. Taylor [10,11]

- Longitudinal assessment
- Emotional impact of OS diagnosis
- Identify factors predicting poorer PRO

Analyst commenced January 2025

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Conclusions

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- Through generous funding, the infrastructure provided by a clinical trial centre, expertise of multi-disciplinary team and collaboration across the UK it has been possible to recruit a cohort of osteosarcoma patients to address clinical and biological questions

- The study provides opportunities

  → to exploit data and tissue collection

  → leverage additional funding

  → Support clinical and academic research and researchers

  → unique resource for the community

Maximising benefits for patients, clinicians and researchers

CANCER RESEARCH UK | CANCER TRIALS CENTRE | UCL

Acknowledgments

BCRT and Hamilton Family

The Patients and Carers

ICONIC Coinvestigators, Research Nurses, PIs and Collaborators

Bernadette Brennan, Manchester Children's Hospital, Chair NCRI
Craig Gerrand, RNOH
Adrienne Flanagan, UCL and RNOH
Kenny Rankin, Newcastle
Robin Young, Sheffield Hospitals NHS Trust
Michael Parry, ROH
Jonathan Stevenson, ROH
Jenny Sherriff, QE II, Birmingham
Dominique Heymann, Sheffield and Nantes
Rachel Taylor, UCL
Lorna Fern, UCLH
Isidro Cortes, EMBL-EBI.
Lucia Cottone, UCL
Filipa Vance, PPI

Phillip Green, GP and PPI
Peter Lloyd, PPI

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Sharon Forsyth, Krystyna Reczko,
Kate Sparksman, Molly Richardson
Rubina Begum
Will Wilson Statistician

FOSTER
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Marie-Cecile Le Deley
Antonin Marchant

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Northern Ireland: Helen McCarty
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Nischalan Pillay, UCL Cancer Institute
Carolyn Langford, R&D, ROH
Paul Cool, RJAH, Sarah Pratap, Oxford
Peter Simmonds, Southampton
Han Wong, Addenbrooke's
Quentin Campbell-Hewson, Newcastle
Matthew Pugh, Birmingham, Emine Hatipoglu, UCL.
Sergio Quezada, UCL, Geoff Parker UCL, Sam Behjati, Sanger Institute,