

# NCRI Sarcoma Group Priorities 2023 - 2026



## NCRI Partners

NCRI is a UK-wide partnership between research funders working together to maximise the value and benefits of cancer research for the benefit of patients and the public. A key strength of NCRI is our broad membership with representation across both charity and government funders as well as across all four nations in the United Kingdom.



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## Introduction

The NCRI Groups bring the cancer research community together to develop practice-changing research, from basic to clinical research and across all cancer types, supporting NCRI's strategy. The NCRI Sarcoma Group is a multi-disciplinary community of researchers and consumers focused on developing research to improve outcomes for sarcoma cancer patients.

Each NCRI Group engages in a prioritisation process to identify the priority areas in its area of research (Appendix A). This process dictates the work of the group as well as providing an assessment of the state of research for the wider research community.

The NCRI Sarcoma Group has identified its research priorities working with members of the research community and NCRI Partners. Full details of the meetings held can be found in Appendix B and a list of participants can be found in Appendix C.

There are multiple areas the NCRI Sarcoma Group has identified as priorities, an overview of which can be seen below with full details on pages 10-12 of this document. The Group will initially focus on priorities 1-4, forming time-limited working groups to address these priorities. When one working group finishes, capacity will be transferred to address the next task in this priority. An overview of the NCRI Sarcoma Group structure can be found on page 6.

The strategies of NCRI Groups will be refreshed every three years. In addition, the research landscape will continue to be routinely assessed by NCRI to ensure the most pressing questions in the sarcoma research landscape are addressed over the course of this three-year strategy.

### NCRI Sarcoma Group strategic priorities at a glance

1. Develop a Soft Tissue Sarcoma (STS) trial for all patients.
2. Develop studies into treatment of metastatic chondrosarcoma.
3. Extend and build on the ICONIC osteosarcoma study.
4. Build on the Rhabdomyosarcoma: The open Frontline and Relapsed Rhabdomyosarcoma (FaR-RMS) study to facilitate further investigation of important research questions in the field.
5. Develop a study into treatment of Nonrhabdomyosarcoma.
6. Further develop the Multi-Arm Sarcoma Surgical (MASS) trial.

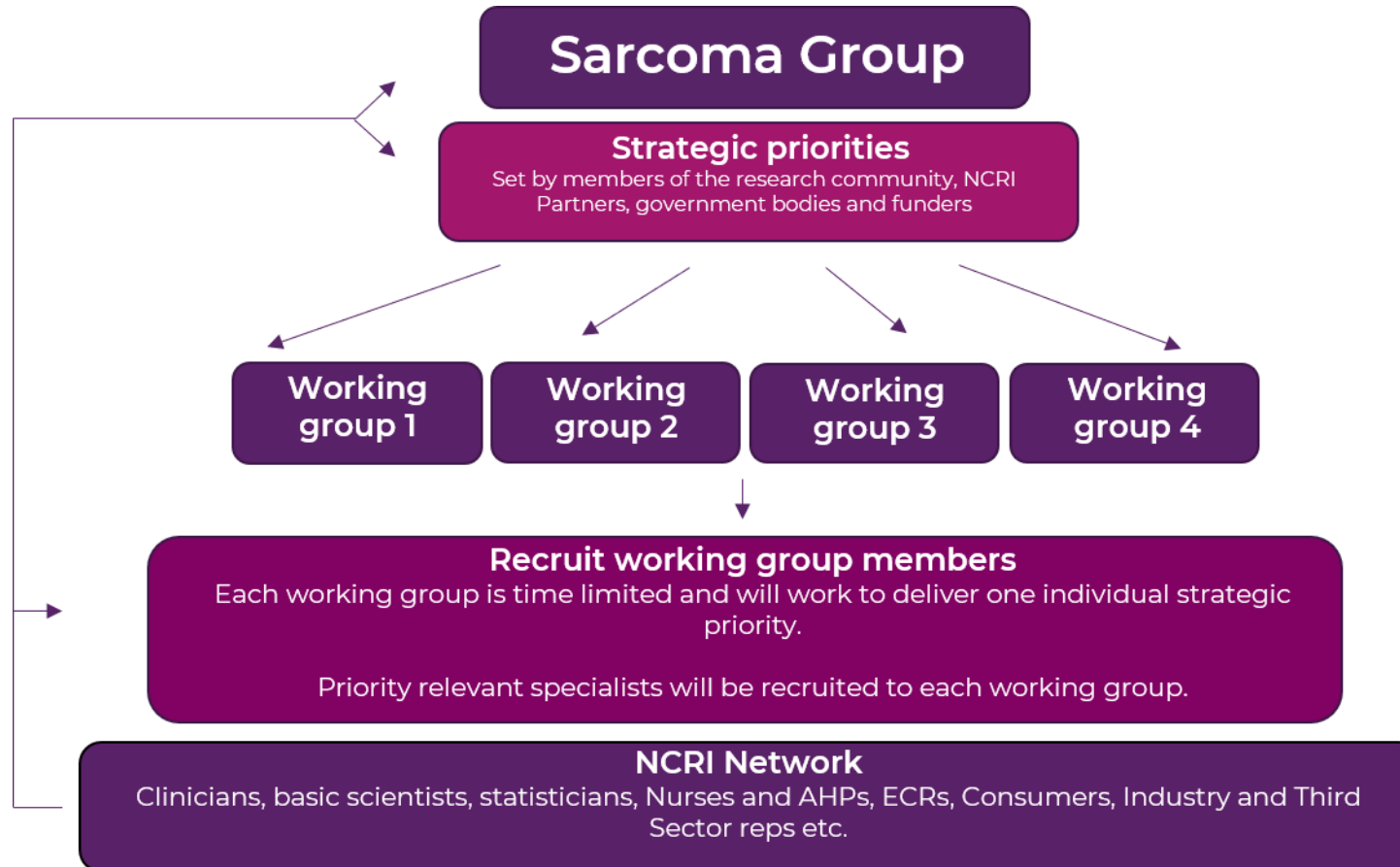


“The Sarcoma Group brings together clinicians, scientists and Consumers to work on the key research areas of these rare tumours. The Group strategy day held in November 2020 focused on key areas and themes in sarcoma research, including interventional therapeutic trials to improve outcomes in soft tissue sarcoma, quality of life (QOL) and patient reported outcomes (PROMS), as well as cross-cutting research into surgical intervention as part of large, randomised trials.

A common theme in the discussions and hence in the subsequent Sarcoma Group strategic priorities is the necessity of international collaboration in research projects and trials due to the rarity of these sarcomas. The priorities also demonstrate the evolution of trials and their results into further studies, building new questions into our platform studies such as Far-RMS. The rarity of our tumours demands novel statistical plans such as Bayesian methodology which we will continue to expand into our trials. We look forward to building on the work of the Sarcoma Group thus far and addressing the major challenges in the field over the coming years.”

**Prof Bernadette Brennan, Chair of NCRI Sarcoma Group**

## NCRI Sarcoma Group structure at a glance



# NCRI Sarcoma Working Groups

## Initial working groups in set up

The Sarcoma Group has identified 6 strategic priorities, full details of which can be found on pages 10-12 of this document. Time-limited working groups will be set up to address the first four priorities for the Sarcoma Group, each of which are outlined below. Once one working group reaches completion, capacity will be transferred to the next priority

### Working group 1

#### Develop a Soft Tissue Sarcoma (STS) trial for all patients

The aim of this priority is to develop a change in practice in how high-risk STS is described and how best to investigate new treatments through a collaborative platform of clinicians, scientists, and pathologists. The primary clinical objective of this project is to determine variation of treatment across the UK in all age high-risk STS and use this information to inform new therapeutic and management strategies. We aim to understand the biological and clinical factors which define high-risk STS and paediatric Non-Rhabdomyosarcoma Soft Tissue Sarcoma (NRSTS), to predict the development of metastatic disease, and hence improve outcomes and treatment. The proposed title of this study is BIOSARC: Understanding the biology of soft tissue sarcomas. The objectives of this study are to:

- Identify novel genetic and immune tumour biomarkers through multi-platform analyses.
- Correlate molecular characteristics with clinical outcomes to identify patients at higher risk and help identify new treatment targets.
- Determine the impact of intra-tumour heterogeneity and evolution on treatment response and outcome.

Integral to the success of this priority will be the continued interaction with other ongoing studies such as Panthr-S and STRASS 2.

## Working group 2

### Develop studies into treatment of metastatic chondrosarcoma

Surgery is the mainstay of treatment of chondrosarcoma with good outcomes in localised operable disease, however, the failure of systemic therapy in metastatic disease needs to be addressed. Through this priority we aim to work on opportunities identified at a workshop held with Bone Cancer Research Trust (BCRT) to develop future studies into treatment of metastatic disease, including exploring opportunities to develop research into early diagnosis, as well as the potential to engage with up-and-coming studies involving new targeted agents under development in both the commercial and academic sector. Potential studies to consider include INBRX, a phase 2 study of INBRX-109 in unresectable or metastatic conventional chondrosarcoma patients, and IMMNUOSARC, a European collaborative study with a cohort open for dedifferentiated chondrosarcoma.

A study for chondrosarcoma has been strategised to align with the priority set for development of a surgical study, as was discussed at the sarcoma strategy day. Dr Rankin has developed a proposal, SarcoSIGHT, with an application for funding under review. A follow up study to the detection of IDH mutations in blood of chondrosarcoma led by Prof Flanagan has been discussed, pending the results of the study, which are imminent. A task and finishing group have been proposed to develop this further.

## Working group 3

### Extend and build on the ICONIC osteosarcoma study

The ICONIC (osteosarcoma) study, developed through the former Bone Subgroup of the NCRI Sarcoma Group, has progressed very well despite some delays due to COVID-19. The study is open in 23 centres across the UK including paediatric, TYA, adult and surgical centres. To improve outcomes, including lack of events, deaths and improved quality of life, the ICONIC research group plan to extend and build on this study through this working group with a new application in draft. This would allow for exploring variation in practice in elderly patients and developing chemotherapy questions in this group. There will be multiple work packages in this application developed from the ICONIC study including clinical outcomes/quality of life; imaging biomarkers; and biology focused on immunology/tumour microenvironment. The group are applying for Bone Cancer Research Trust Hamilton £1 million fund to continue adding questions to the ICONIC study.

ICONIC will feed into development of research objectives of the FOSTER consortium and eventually will lead to an overarching clinical trial in osteosarcoma in Europe delivering new therapies, collecting biological samples and developing biomarkers with outcomes beyond survival, such as quality of life.



## Working group 4

Build on the Rhabdomyosarcoma: The open Frontline and Relapsed Rhabdomyosarcoma (FaR-RMS) study to facilitate further investigation of important research questions in the field

The FaR-RMS study was developed by the former Young Onset Soft Tissue Sarcoma Subgroup of the NCRI Sarcoma Group in 2018 and will run for at least 10 years, including follow up. Whilst this is an 'all ages' study, the predominant focus is on children and young adults and remains a priority of the Sarcoma Group with the UK leading on much of this international study. This working group will focus on developing this platform study, facilitating further research questions beyond the current 9 randomisations. Questions in development within NCRI Sarcoma Group include:

- Liquid biopsy – developing prognostic biomarkers and detecting early recurrence.
- High Risk Quality of Life (HRQoL) – looking at outcomes of interventions beyond survival.
- Novel Targets for relapsed and upfront RMS – bringing in new therapies to form new arms of the trial.
- Imaging biomarkers – identifying new biomarkers to use within the trial engaging radiology and imaging researchers in the UK.
- Radiotherapy Quality Assurance (Proton, Photon and Brachytherapy) – improving the quality of radiotherapy and the impact this has on outcomes, for example, reducing side effects.
- Translational research – exploring the combination of targeted therapy and radiotherapy for RMS and other fusion driven sarcoma for future trial arms.

## NCRI Sarcoma Group strategic areas in full

### Priority 1: Develop a Soft Tissue Sarcoma (STS) trial for all patients

The aim of this priority is to develop a change in practice in how high-risk STS is described and how best to investigate new treatments through a collaborative platform of clinicians, scientists, and pathologists. The primary clinical objective of this project is to determine variation of treatment across the UK in all age high-risk STS and use this information to inform new therapeutic and management strategies. We aim to understand the biological and clinical factors which define high-risk STS and paediatric Non-Rhabdomyosarcoma Soft Tissue Sarcoma (NRSTS), to predict the development of metastatic disease, and hence improve outcomes and treatment. The proposed title of this study is BIOSARC: Understanding the biology of soft tissue sarcomas. The objectives of this study are to:

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- Correlate molecular characteristics with clinical outcomes to identify patients at higher risk and help identify new treatment targets.
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Integral to the success of this priority will be the continued interaction with other ongoing studies such as Panthr-S and STRASS 2.

### Priority 2: Develop studies into treatment of metastatic chondrosarcoma

Surgery is the mainstay of treatment of chondrosarcoma with good outcomes in localised operable disease, however, the failure of systemic therapy in metastatic disease needs to be addressed. Through this priority we aim to work on opportunities identified at a workshop held with Bone Cancer Research Trust (BCRT) to develop future studies into treatment of metastatic disease, including exploring opportunities to develop research into early diagnosis, as well as the potential to engage with up-and-coming studies involving new targeted agents under development in both the commercial and academic sector. Potential studies to consider include INBRX, a phase 2 study of INBRX-109 in unresectable or metastatic conventional chondrosarcoma patients, and IMMUNOSARC, a European collaborative study with a cohort open for dedifferentiated chondrosarcoma.

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### Priority 3: Extend and build on the ICONIC osteosarcoma study

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#### **Priority 4: Build on the Rhabdomyosarcoma: The open Frontline and Relapsed Rhabdomyosarcoma (FaR-RMS) study to facilitate further investigation of important research questions in the field**

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#### **Priority 5: Develop a study into treatment of Nonrhabdomyosarcoma**

This rare group of tumours includes a wide variety of histological subtypes, and research initiatives have often involved registry type studies, which are hard to fund in the UK. There has been no study available since the closure of the European Soft tissue Sarcoma Group (EpSSG) Non-Rhabdomyosarcoma Soft Tissue Sarcoma (NRSTS) 2005 study in 2016, so it is a key area of need. These studies would include children/teenage and young adults (TYA) but could be extended to all ages.

Current initiatives include the following:

- EpSSG Molecular Identification and Characterisation of NRSTS in Kids, Adolescents and Young Adults (MYKIDS).
- EpSSG High Risk NRSTS study proposing to investigate the combination of Regorafenib with ifosfamide doxorubicin chemotherapy for high risk NRSTS. There are proposals for molecular and imaging biomarkers. To develop a phase Ib study first then randomised phase II/III.

#### **Priority 6: Further develop the Multi-Arm Sarcoma Surgical (MASS) trial**

Previous work from the Sarcoma Group to address a lack of trials led to the proposal of the Multi-Arm Sarcoma Surgery (MASS) trial. This trial addresses the following three randomised areas:

- Peri-operative therapies with Cox inhibitor/ $\beta$  blocker to reduce metastatic rate.

- SarcoSIGHT assessing fluorescence guided surgery to reduce positive surgical margins.
- SUNstudy assessing negative pressure dressings to reduce wound complications.

This working group will further develop this trial by exploring the design and funding of the study with Cancer Clinical Trials Unit, Scotland (CaCTUS). The sarcoSIGHT arm of the trial has already been submitted to NIHR for funding which will not preclude further funding applications for the whole trial going forwards with this MAMS design.

## **NCRI Cross-cutting priority**

### **Identify barriers resulting in a lack of diversity in clinical trials and propose solutions to improve equality, diversity, and inclusion.**

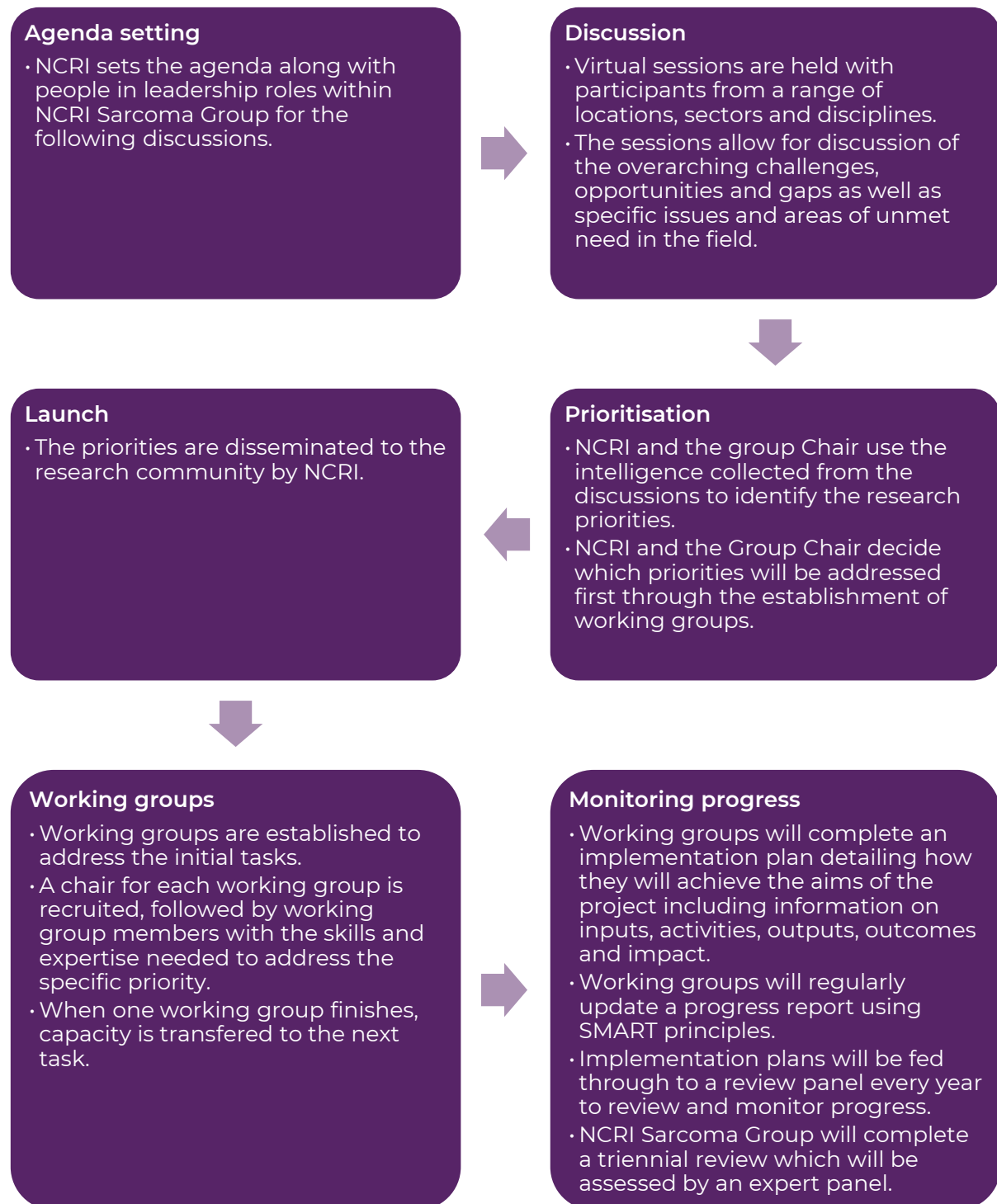
Barriers resulting in a lack of diversity in clinical trials across cancer types has been raised as an issue in many of NCRI's discussions with researchers. For this reason, this priority will be addressed collaboratively in a working group comprising experts from across NCRI Groups. This priority aims to establish the reasons behind a lack of diversity in clinical trials and provide solutions to increase participation of a diverse cohort of patients in future studies. A working group will address the common issues across the board, as well as identifying cancer-type specific barriers, and produce guidelines on the steps to take to improve the inclusion of patients from a range of backgrounds into clinical trials from their inception. More details on this working group will be decided in due course.

## Next steps

Working groups addressing the highlighted tasks are currently being formed. These groups will be made up of the experts needed to address each research question. To be the first to hear about opportunities to join these working groups please sign up to the [NCRI Sarcoma Network](#). The progress of these working groups will be published in the annual reports and triennial review of NCRI Sarcoma Group. These can be found on the [NCRI website](#). Members of the NCRI Sarcoma Network will also be updated periodically on the progress of the group.

Please [get in touch](#) if you have any questions or comments regarding this report or if you are interested in joining one of the [NCRI Networks](#), the [NCRI Consumer Forum](#) or our [NCRI Early Career Researcher Forum](#).

**Appendix A**  
**NCRI Sarcoma Group priority setting process**



## Appendix B

### NCRI Sarcoma Group priority discussion sessions 2020

The NCRI Sarcoma Group strategy day, held in November 2020, attracted 60 participants from a variety of sectors and disciplines, including NCRI Consumer Forum members, early career researchers and NCRI Partners. The introductory presentation allowed for discussion of the overarching strategic and funding opportunities in sarcoma research, whilst the subsequent sessions on soft-tissue sarcomas, surgery and patient reported outcomes saw presentations from a range of experts, including international expertise, setting the scene for breakout discussions to identify and decide on a way forward to collaboratively meet the most pressing needs in sarcoma research today.

## Sarcoma Group Strategy Day Agenda

**Friday 27<sup>th</sup> November 2020**

**Chair: Prof Bernadette Brennan**

### Session 1: Strategy updates

Speakers:

- Aims – **Prof Bernadette Brennan**, Royal Manchester Children's Hospital
- NCRI strategic priorities – **Dr Ian Lewis**, NCRI
- Sarcoma research funding landscape – **Dr Ian Lewis**, NCRI
- Strategy and funding opportunities
  - Sarcoma UK – **Dr Sorrel Bickley**, Sarcoma UK
  - Bone Cancer Research Trust - **Dr Zoe Davidson**, Bone Cancer Research Trust
  - Cancer Research UK – **Dr Maria Antonietta Cerone**, Cancer Research UK

### Session 2: Soft Tissue Sarcoma

Speakers:

- Overcoming pitfalls and challenges to deliver a national STS proposal – **Dr Aisha Miah**, Royal Marsden NHS Foundation Trust.
- Building on the success of the CRUK Accelerator Award – **Prof Robin Jones**, Royal Marsden NHS Foundation Trust & **Dr Paul Huang**, Institute of Cancer Research (ICR)

Discussion:

Outline of a clinical study in STS (interactive session) – **All attendees**

### Session 3: Surgery

Chair: **Mr Kenny Rankin**, Newcastle University

Speakers:

- Perioperative drugs in sarcoma – **Dr Pan Pantziarka**, Anticancer Fund.
- sarcoSIGHT- fluorescence guided NIHR surgical trial – **Mr Kenneth Rankin**, Newcastle University
- Implant coatings to prevent infection trial – **Mr Jonathan Stevenson**, Royal Orthopaedic Hospital NHS Foundation Trust
- Negative wound pressure for sarcoma trial – **Mr Sanjay Gupta**, NHS Greater Glasgow & Clyde.

### Session 4: Patient reported outcomes – purposes and tools

Chair: **Mr Roger Wilson**, Sarcoma UK

Speakers:

- Setting the scene – **Mr Roger Wilson**, Sarcoma UK
- Principles and Approaches – **Prof Melanie Calvert**, University of Birmingham
- Tools and Techniques – **Dr Olga Husson**, Netherlands Cancer Institute

## Appendix C Strategy day and NCRI Sarcoma Group contributors

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**Mr Piers Gaunt,**  
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NHS Greater Glasgow &  
Clyde

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Netherlands Cancer  
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**Dr Paul Huang,**  
Institute of Cancer  
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**Prof Lee Jeys,**  
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**Prof Robin Jones,**  
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**Dr Alexander Lee,**  
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**Dr Henry Mandeville,**  
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**Dr Kieran McHugh,**  
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**Dr Magdalena Meissner,**  
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**Dr Christina Messiou,**  
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**Dr Aisha Miah,**  
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**Mr Roger Wilson,**  
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**Ms Rachel Laurence,**  
National Cancer  
Research Institute

### **NCRI Sarcoma Group contributors**

The following Sarcoma Group members were unable to attend the strategy day but have contributed to the direction of the Sarcoma Group's strategic priorities through their involvement with the Group and former Subgroups.

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