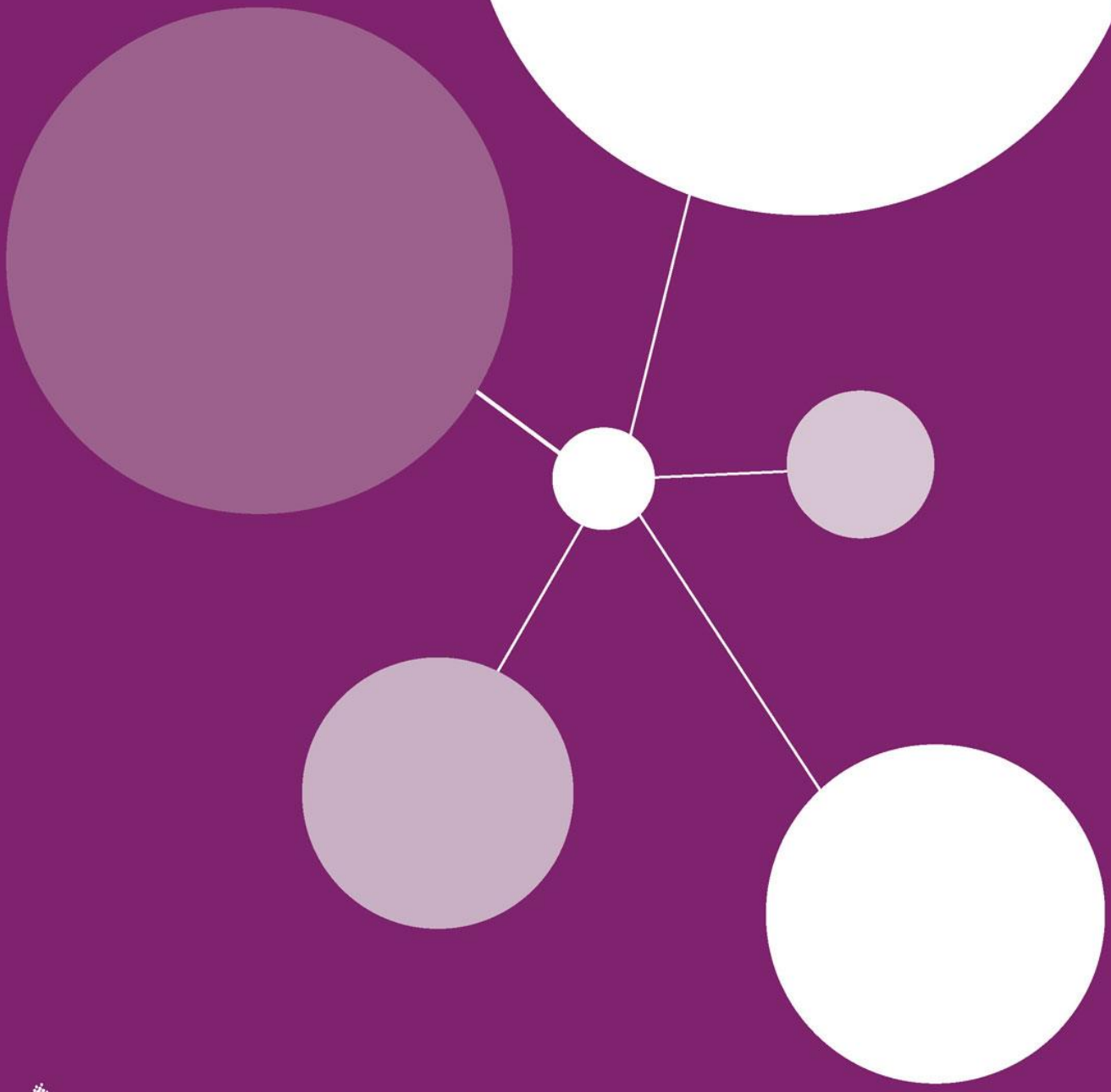
NCRI
National
Cancer
Research
Institute

NCRI Sarcoma Clinical Studies Group

Annual Report 2017-18



Partners in cancer research

NCRI Sarcoma CSG
Annual Report 2017-18

1. Top 3 achievements in the reporting year

Achievement 1

Achieving funding for ICONIC from Bone Cancer Research Trust (BCRT): Improving outcome through Collaboration in OsteosarComa

Funding: Details are as follows:

- Dr Sandra Strauss (Chief Investigator), Professor Jeremy Whelan, Professor Bernadette Brennan, Mr Craig Gerrand, Flanagan A et al,
- Funder: BCRT
- Sponsor: University College London Cancer Trials Centre (UCL CTC)
- Sum: £449,631.79

Trial summary: The purpose of this programme is to deliver a step-change in our approach to seeking better treatments for osteosarcoma (OS) by establishing a clinically annotated cohort of newly diagnosed patients with OS with longitudinal collection of bio-specimens to serve as a platform for biological studies.

Achievement 2

Opening the first portfolio study on chondrosarcoma, which is now open in four of the five primary bone sarcoma centres. Does circulating DNA predict the grade and disease burden of chondrosarcoma? The nationwide collaboration study details are: -

- Investigators: Professor Adrienne Flanagan (CI), Professor Lee Jeys & Mr Craig Gerrand
- Funder: BCRT
- Sum: £69,963
- Sponsor: Royal National Orthopaedic Hospital, London
- Design: Observational study with biological arm
- Trial Period: 13/10/2017 – 01/11/2020

- Recruitment: 29/130 patients, on target

Trial summary. This study looks at circulating IDH1 mutations in the blood of patients with chondrosarcoma, and aims to correlate with the final pathological diagnosis. It also proves the principal that multicentre collaboration is feasible in this condition and is a platform on which to develop further studies.

Achievement 3

Achieving funding for FaR-RMS: A multi-arm-multistage study for children and adults with localised and metastatic Frontline and Relapsed Rhabdomyosarcoma.

Funding: Details are as follows:

- Dr Meriel Jenney (CI), Dr Julia Chisholm, Dr Henry Mandeville., Professor Keith Wheatley., Merks H et al.; CRUK/17/011 FaR-RMS: A multi-arm-multistage study for children and adults with localised and metastatic Frontline and Relapsed RhabdoMyoSarcoma. January 2018 - December 2028
- Funder: Cancer Research UK (CRUK)
- Sum: £2,330,159.53

Trial summary: The FaR-RMS Study is an overarching clinical trial that explores several aspects of treatment for RMS, both for patients newly diagnosed with the disease and also at the time of relapse. It is open to patients of all ages (children, teenagers and young adults (TYA) and adults) across Europe who are newly diagnosed with RMS or in whom the disease recurs.

2. Structure of the Group

The membership of the Sarcoma CSG has evolved since 2016 and the Group is extremely welcoming, collegiate and engaging. Unlike many CSGs, the number of research active clinicians working in the field of sarcoma is limited and thus the number of suitable members is also limited, resulting in several members sitting on the committee for many years. This brings with it great experience of opening and running large trials, however, encouraging younger members of the community to develop trials for the future is also fundamental for the longer-term success of the CSG. The Group remains dynamic and productive, being on course to deliver the objectives set after the strategy day held in 2016.

Dr Helen Hatcher, Professor Jeremy Whelan, Miss Ray Davis and Dr Alexander Lee rotated off the group and were thanked for their hard work and contributions made whilst members of the Group.

This year the CSG welcomed new members: Professor Sue Burchill, Dr Louise Carter and Professor Luc Bidaut.

3. CSG & Subgroup strategies

Main CSG

Increase the number of trials available for sarcoma patients in the UK

This reporting year the portfolio has seen the funding or opening of several studies developed with or by the CSG which will increase the number of trials open to sarcoma patients. Important studies have been opened in Chondrosarcoma and Chordoma, both of which have started with good initial recruitment. Euro-Ewings remains an important large randomised international study with 179 patients recruited within the UK. The recent funding of the ICONIC study means that when this opens, there will be a study for all major types of bone cancer for patients, which is a massive achievement. There are also a number of new studies for relapsed bone sarcoma.

The major advance has been the initialisation of phase II of Sarcoma Assessment Measure (SAM), a large study for all sarcoma patients which plans to recruit 1000 patients. There have been several new phase I/II studies open for patients with soft tissue sarcoma (STS) open this year, including for the most common STS subtype, undifferentiated pleomorphic sarcoma and several studies for advanced disease in STS. An industry sponsored phase III study is also available for patients with advanced disease.

Develop new trials with both interventional and non-interventional arms and allow as many patients with sarcoma to enter data into studies

The CSG has worked hard to develop three major bone studies with observational and translational arms in osteosarcoma, chondrosarcoma and chordoma, all of which have been funded and 2 are open. FaR-RMS and EpSSG NRSTS 2018 studies will have both interventional and translational arms for TYA and paediatric patients. SARC MET trial is still in development by the Lung Mets Working Party and plans to have both interventional and non-interventional elements in an attempt to make the study available to all patients with metastatic STS.

Increase studies in bone sarcoma

The Bone and YOSS Subgroups, together with the main CSG have done an excellent job in:

- Obtaining significant funding for the ICONIC study for osteosarcoma, in the lack of a successor study to EURAMOS. A study which will aim to recruit all patients in UK with Osteosarcoma and has a strong translational element.
- Opening the study 'Does circulating DNA predict the grade and disease burden of chondrosarcoma? A nationwide collaboration study'. The first portfolio study in chondrosarcoma with a strong translational arm and encourages the 5 bone sarcoma MDTs in England to collaborate and share tissue. This study will also recruit patients with benign enchondromas to study the link between the pre-malignant condition and chondrosarcoma.

- Opening the Guiding Chordoma Treatment Through Molecular Profile which again has a large translational arm and is open to all patients irrespective of stage in this rare condition.
- Continuing to support the multiple studies in Ewing's sarcoma, including the large international randomised studies, EUROEWING and rEEcur. There are also some stand-alone translational studies open for Ewing's sarcoma.

The three new studies mean that there is now a study open for every major bone sarcoma subtype and the SAM study is open for all bone sarcomas.

Further develop the Sarcoma CSG portfolio

The CSG is in the process of developing a Soft Tissue Sarcoma Subgroup, with Dr Aisha Miah as Chair and good engagement from both within and without the CSG. The CSG is confident this Subgroup will develop further over-arching trials in STS which are needed. The Lung Mets Working Party is developing SARC-MET study which has been under extensive discussion within the CSG, and should be submitted for funding in 2018.

A key strategic aim for the CSG following the Strategy Day was to develop studies which gave opportunity for the whole sarcoma community to take part in trials the opening of the new bone sarcoma trials and Sarcoma Assessment Measure trial have given this opportunity. The opportunity to further develop STS trials through a new STS Subgroup will also enhance this aim. The CSG was also cognisant to ensure new trials had strong translational arms and again this has been the case. Another priority was to engage with the limited number of sarcoma MDTs in the UK to develop a sarcoma research network, the ICONIC, Chondrosarcoma and Chordoma trials deliberately have collaboration at their heart and often study title to achieve this goal.

The CSG has changed the structure of the main meetings to give ample time for trial development and updates. The Group has invited investigators of studies developed outside the main CSG to present their proposals prior to submission to the CSG for feedback, awareness and endorsement of the CSG. The CSG has also regularly invited funder representatives from CRUK, Sarcoma UK and BCRT to attend meetings to try to harmonise future applications with research calls, to maximise the chance of successful application and allow a two-way dialogue with funders.

Raise awareness and profile

The CSG has a regular section at the British Sarcoma Group (BSG) to disseminate the new trial ideas and studies which are opening, this also allows the CSG to engage with the sarcoma community to uncover areas of unmet research need from the sarcoma community. The interaction between the NIHR Sub-Specialty Leads (SSLs) and the CSG has been variable and sometimes problematic. Highlights from the CSG meeting are disseminated to the SSLs and there have been attempts to hold meetings with the SSLs and invite them to the main CSG meeting, however, this has been with limited success. One of the main issues is that the Sarcoma SSL is not always a sarcoma clinician in some CRNs and that a significant number of Sarcoma SSL positions remain unfilled. The CSG requires engagement with the SSLs to ensure adequate uptake of new trials on the portfolio, however, due to centralisation of care, the number of units recruiting to portfolio studies is limited. The CSG therefore encourages the

chief investigation or trial management group of portfolio studies to liaise directly with units that are recruiting to studies; this has been successful so far.

The early results of trials have been presented at important scientific meetings such as the American Society of Clinical Oncology (ASCO), Connective Tissue Oncology Society (CTOS), NCRI and BSG. The CSG continues to publish the results of trials in high impact journals.

Develop trials in key research priority areas

The CSG is proud that of the research ideas developed at the Strategy Day, new trials have been funded or opened in all the major areas which were felt to be key. The more problematic areas of surgical trials, follow up studies and more STS trials require further work. The CSG has tried to embed surgical questions into larger studies, such as ICONIC, where surgical margin validation in the context of response to chemotherapy is a major part of the study, together with radiological estimation of response to chemotherapy. The Group is aware of areas which require development and hope that SARC-MET will obtain funding in the near future to fulfil another key research area.

A number of small and medium size trials are currently open on the portfolio, with 5 industry trials undergoing adoption/set up currently and the CSG has engaged with industry, recently the AZ Alliance, to identify possible novel agents for soft tissue sarcoma, with 2 trial proposals presented at the last meeting in May.

Strengthen UK wide and international working

Given the size of the national and international community the CSG has always benefitted from close links with national and international organisations. This is clearly seen within the studies in the portfolio and in development. The CSG has representatives on key research organisations such as European Organisation for Research and Treatment of Cancer (EORTC), Children's Oncology Group (COG), Scandinavian Sarcoma Group (SSG), European paediatric Soft tissue sarcoma Study Group (EpSSG), Euro Ewing Consortium (EEC), IOC and Chordoma Foundation. This remains a strong and important priority for the CSG.

The CSG also regularly interacts with other NCRI groups with members sitting on Consumer Forum, SPED Advisory Group and Teenage & Young Adult (TYA) & Germ Cell Tumours (GCT) CSG and Dr Sandra Strauss is the Sarcoma Site Specific Clinical Reference Group (SSCRG) Chair for National Cancer Registration and Analysis Service (NCRAS) for sarcoma. The CSG has benefitted from interaction with Children's Cancer & Leukaemia CSG, Gynaecological Cancer CSG, Primary Care CSG, Psychosocial Oncology & Survivorship CSG, Supportive & Palliative Care CSG and TYA & GCT CSG either in the main meetings or via interaction with subgroups.

The CSG has excellent links with the sarcoma community within the UK. The CSG annually presents current research projects and trials ideas at the annual BSG meeting, which is a multidisciplinary group of clinicians and consumers, to gain feedback for trial ideas, publicise trials and their results. The CSG has presented trial results at ASCO, NCRI Conference and

CTOS. Members of the CSG also regularly contribute to consumer conferences for Sarcoma UK, BCRT and Sarcoma Patients EuroNet (SPAEN).

CSG structure and function

The current core membership includes 22 members from a variety of backgrounds relevant to sarcoma research. The group currently consists of 3 clinical oncologists, 4 medical oncologists, 3 orthopaedic oncology surgeons, 2 paediatric oncologists, 2 consumer representatives, 2 trainee representatives (a clinical oncologist and clinical research fellow – both with a strong background in basic science research), a medical physicist (with expertise in imaging), a pathologist, a sarcoma specialist nurse, a sarcoma scientist, a statistician and a trial co-ordinator.

The strength of the CSG lies in the diversity of its membership; with several members holding academic positions undertaking basic science research, as well as clinical positions, thus giving expertise for both clinical and biological research. Several of the members have been involved in devising, gaining funding, running and concluding large national and international trials, which serves as a great inspiration and an invaluable resource for the group. Representatives of two of the main charitable funders of sarcoma research, Sarcoma UK and BCRT, attend the meeting, which provides valuable feedback to the members and helps the charities consider areas of unmet research needs. The CSG regularly debate the skills within the group and areas which could be strengthened. The Chair has pro-actively approached several individuals with skills in areas under-represented and encouraged them to apply for to join the CSG or subgroups.

Patient and Public Involvement and Impact

The consumer involvement within the CSG remains good with Mr Michael Maguire being the current the consumer representative, as Miss Ray Davies had to withdraw from the CSG due to a career move abroad. Former consumer member Mr Roger Wilson CBE remains a scientific advisor to the CSG and former consumer member Mr Robert Wensley remains a member of the NCRI Consumer Forum. Both Roger and Michael have been involved in the development of studies with the last year, as well as being active in the NCRI Consumers Forum 'Dragons Den'. The CSG is aware that having at least one consumer who is a sarcoma patient rather than a care giver would be advantageous. The CSG has worked with Sarcoma UK and BCRT to identify patients active in their organisations that may be suitable to join the CSG and subgroups. The CSG is hopeful for a positive response to the current advert for consumer members.

Bone Tumour Subgroup (Chair, Mr Craig Gerrand)

Develop studies in bone sarcoma through wide engagement, including involvement with charitable partners and national collaboration

By widening participation in the Subgroup, with the support of BCRT, we have been able to increase engagement and support the development of new studies. This approach of opening the doors has been successful and means there is a wide range of members with a breadth of experience that covers the areas necessary for translational medicine, drug trials and TYA trials. We have had surgical and pathology engagement to good effect leading in particular to a new study in chondrosarcoma which has recently opened. The Subgroup has also recently developed the ICONIC study for osteosarcoma, in the absence of an international follow on study to EURAMOS. This study aims to recruit all patients with osteosarcoma in the UK and was a key strategic aim of the CSG following the strategy meeting. This proposal has been developed in consultation with BCRT, the key funder, and has recently been funded and subsequently adopted in the near future. This proposal also supports a large translational component, separately funded through a large charitable donation. The ICONIC, Chondrosarcoma and Chordoma studies have all benefitted from this new collaborative strategy.

Develop studies where there were none, for osteosarcoma and chondrosarcoma

The ICONIC osteosarcoma study was part funded by BCRT to the sum of £ 449,631.79, with separate funding achieved from the Tom Prince Trust for the translational element. The study is being sponsored by the UCL CTU and should open in 2018.

The first portfolio study on chondrosarcoma is now open in four of the five primary bone sarcoma centres. Does circulating DNA predict the grade and disease burden of chondrosarcoma? A nationwide collaboration study received £69,963 funding from BCRT and has already recruited 29/130 patients having only been open for a few months. Work developing a successor study for this study will need to begin soon.

Promote national collaboration in the development and delivery of studies

The studies described above are both multicentre, national proposals which the Subgroup has encouraged, with investigators and study delivery in more than one centre. The word collaboration appears in the title of both ICONIC and the Chondrosarcoma study as this was a major strategic aim of the Subgroup and CSG. Engagement from all the bone sarcoma centres has been excellent thus far.

Young Onset Soft tissue Subgroup (Chair, Professor Bernadette Brennan)

Open a first line study in Rhabdomyosarcoma across all ages and 2. Build in current relapse studies in RMS using VIT as the backbone

These two strategic aims have progressed with the submission and successful funding by the CRUK of FaR-RMS: A multiarm-multistage study for children and adults with localised and metastatic Frontline and Relapsed Rhabdomyosarcoma (in set up).

Trial summary: The FaR-RMS Study is an overarching clinical trial that explores several aspects of treatment for RMS, both for patients newly diagnosed with the disease and also at the time of relapse. It is open to patients of all ages (children, TYA and adults) across Europe who are newly diagnosed with RMS or in whom the disease recurs.

To develop an all age European study in specific soft tissue which occurs in paediatric, TYA and adult age group e.g. Synovial Sarcoma, MPNST, leiomyosarcoma and liposarcoma

There is a trial in early development within Europe to examine the role of Olaratumab in addition to ifosfamide and doxorubicin in high risk soft tissue sarcomas, which will lower the traditional age limit of 18 to include TYA and paediatric subjects.

Build on the outcomes of other rare sarcomas from the NRSTS study to develop further clinical trials, specifically Rhabdoid tumours at all sites and synovial sarcoma

This will be progressed by developing further clinical trials.

EURO RHABDOID 2018 (study in planning):

- Initial discussion re sponsorship and trial development with Birmingham Children's Cancer CTU
- Planned countries: UK, France, Spain, Netherlands, Sweden, Norway, Denmark, Belgium, Ireland, Slovakia, Czech Republic and Italy.
- Internationally developed as part of the European Paediatric Soft Tissue Sarcoma Group (EpSSG)

Title: A phase Ib/II study evaluating the addition of a new agent X in children and adolescents with high risk malignant rhabdoid tumours (MRT) or atypical teratoid/rhabdoid tumours (AT/RT) at diagnosis.

To embed biological studies, biomarkers and novel targets into clinical trial portfolio

This will be achieved in FaR-RMS as above and EpSSG NRSTS 2018 - a successor to EpSSG NRSTS 2005 which will be a prospective cohort study with a biological question, which may be useful for all the NRSTS subtypes.

Increase the TYA population in sarcoma studies

This will be achieved by extending the upper age range for study entry in all proposed studies above

4. Task groups/Working parties

Remit of Gynaecological Sarcomas Working Party

The aim of the Working Party is to gain a better understanding of the different treatments gynae-sarcoma patients receive across the UK. The group wishes to produce guidelines for every gynae-sarcoma patient to be seen by a sarcoma MDT from a gynae-sarcoma questionnaire.

Progress to date

The Working Party has been working in close collaboration with the EORTC Soft tissue and Bone Sarcoma Group. Due to the rarity of this group of tumours the majority of studies require European and International collaboration. A trial is currently recruiting, which is part of the International Rare Cancer Initiative (IRCI) in collaboration with the GOG and EORTC, investigating the role of cabozantinib maintenance therapy in patients with uterine sarcoma who have responded to first line chemotherapy. This is open and recruiting at 4 UK sites. The group have developed a gynae-sarcoma questionnaire, in collaboration with Sarcoma UK, in response to a patient query on the Sarcoma UK support line regarding routine hormone testing on uterine Leiomyosarcoma. Collaboration is anticipated with NCRAS and the NCRAS Gynae Expert Advisory Group. The group also suggested having a gynae sarcoma session at the 2018 BSG meeting, with the bonus that it would attract more pathologists.

Remit of Lung Metastases Working Party

The main focus of this Working Party is to deliver a trial on metastatic sarcoma, the SARC-MET programme.

Progress to date

The Lung Metastases Working Party consists of 3 adult oncologists, a statistician, 2 scientists/epidemiologists with expertise in quality of life outcomes in cancer, a consumer representative, representation from the Supportive & Palliative Care CSG and are currently trying to recruit a health economist.

The trial is being supported by Birmingham Clinical Trial Unit. The trial would aim to determine whether outcomes from metastatic bone and soft tissue sarcoma can be improved by intervention trials of PROM intervention + Standard Oncological Care (SOC) versus SOC alone, with sub studies in minimally invasive techniques vs open surgery techniques to treat pulmonary metastases and timing of systemic therapy. There would also be an overarching assessment of quality of life, cost and geography for metastatic sarcoma care to incorporate into an economic cost analysis of metastatic bone and soft tissue sarcoma. The protocol has been written, discussed at the main CSG meeting and the trial is being aimed towards NIHR funding, however, a smaller feasibility study is planned before major funding is sought. This working party has worked very well and collaboratively with other CSGs to develop this important trial.

5. Funding applications in last year

Table 2 Funding submissions in the reporting year

Cancer Research UK Clinical Research Committee (CRUK CRC)				
Study	**Application type**	**CI**	**Outcome**	**Level of CSG input**
May 2017				
None				
November 2017				
Exploiting circulating miRNAs to predict response and toxicity in patients with Ewing's sarcoma	Biomarker Project Award (Full Application)	Professor Susan Burchill	Not Supported	
Validation of biomarkers for Malignant Peripheral Nerve Sheath Tumour (MPNST) and atypical meningiomas	Biomarker Project Award (Full Application)	Professor Dr Clemens Hanemann	Not Supported	
Other committees				
Study	**Committee & application type**	**CI**	**Outcome**	**Level of CSG input**
CRUK/17/011 FaR-RMS: A multiarm-multistage study for children and adults with localised and metastatic Frontline and Relapsed RhabdoMyoSarcoma. January 2018 - December 2028	CRUK	Dr Meriel Jenney	Successful	• Developed within YOSS Subgroup • Sum: £2,330,159.53 • The approval letter was received in November 2017 and the first patient must be entered within 12 months of this date

				• The grant was activated on 1st February 2018
ICONIC: Improving outcome through Collaboration in OsteosarComa	BCRT	Dr Sandra Strauss	Successful	• Developed within Bone Subgroup • Sponsor: UCL Cancer Trials Centre (UCL CTC) • Sum: £ 449,631.79 • Funded after Interview: 8/3/2017
Molecular characterisation of primary uterine leiomyosarcoma and preclinical investigation of response to non-genotoxic activators of p53 via the MDM2/p53/PPM1D signalling network	Sarcoma UK	Professor John Lunec	Successful	
Towards the production of high potency peptide therapeutics for the treatment of Kaposi's sarcoma	Sarcoma UK	Dr Tracey Barrett	Successful	
Investigating the role and mechanisms of small non-coding RNAs in chondrosarcoma: A small RNA sequencing approach.	Sarcoma UK	Dr Mandy Peffers	Successful	
Linking cellular heterogeneity to therapeutic response in rhabdomyosarcomas	Sarcoma UK	Dr Zoe Walters	Successful	
Characterisation of the Role Of Sarcoma-Associated Fibroblasts in Soft Tissue Sarcoma Development	Sarcoma UK	Dr Will English	Successful	

Utilisation of Genomic mutational signatures in sarcoma for clinical benefit	Sarcoma UK	Dr Nischalan Pillay	Successful	
CIRCUS: A pilot study of CIRCUlating tumour cells in patients with soft tissue Sarcoma	Sarcoma UK	Dr Robin Young	Successful	
Trans-TITAN: Translational analysis of samples from the TITAN (Tumoural Injection of T-VEC and Isolated Limb Perfusion) study	Sarcoma UK	Mr Andrew Hayes	Successful	
Circulating Tumour Cells as Predictors of Disease Progression and Overall Survival in Dogs with Naturally-occurring Osteosarcoma	Sarcoma UK	Prof Matthew Allen	Successful	
Improving soft-tissue sarcoma diagnosis with non-invasive procedures	Sarcoma UK	Prof David Gonzalez de Castro	Successful	
Exploring socio-demographic inequalities in the diagnosis of sarcoma, with a particular focus on deprivation	Sarcoma UK	Dr Richard McNally	Successful	

6. Consumer involvement

Michael Maguire

Michael Maguire is the only current consumer representative as Miss Ray Davies had to withdraw from the CSG due to a career move abroad.

Michael continues to provide consumer involvement within CSG meetings and activities as well as providing easy access to a wider pool of experienced consumers in the NCRI Consumer Forum. With this availability of experience and knowledge to critique, question and add ideas to the group, Michael continually supports a key aim of the CSG, to develop new clinical studies. We look forward to a new consumer joining the CSG in the next round of recruitment to continue this trend.

Michael has and will continue to provide involvement input to the proposal of the VMPRASS study proposal that Dr Paul Huang and Dr Robin Jones are leading on. The proposal was pitched to a group of consumers at the NCRI Consumer Forum's Dragons Den session in March 2018 and was presented at the Sarcoma CSG meeting in May 2018. Michael continues to support the development of a study in the development of follow-up and will continue to work with Mr Jonathan Gregory and Dr Paula Wilson in progressing a study in follow-up.

7. Priorities and challenges for the forthcoming year

Priority 1 Formation of the Soft Tissue Sarcoma (STS) Subgroup to co-ordinate and enhance the development of further studies in STS and champion the SARC-MET study to successful funding.
Priority 2 To successfully oversee the launch of ICONIC study following recent funding to maximise the potential number of centres open and patient recruitment.
Priority 3 To successfully oversee the launch of FaR-RMS. Following the successful funding by the CRUK of FaR-RMS: A multiarm-multistage study for children and adults with localised and metastatic Frontline and Relapsed Rhabdomyosarcoma the trial is in set up and will require significant work to open it in multiple centres
Challenge 1 To set up the STS Subgroup and develop new sarcoma trials to complement current trials on the portfolio.
Challenge 2 To develop SARC-MET trial and obtain suitable funding.
Challenge 3 To develop surgical questions and embed within new trials or develop standalone trials.

8. Appendices

Appendix 1 - Membership of main CSG and subgroups

Appendix 2 – CSG and Subgroup strategies
A – Main CSG Strategy
B – Bone Tumour Subgroup Strategy
C – Young Onset Soft-tissue Sarcoma Subgroup Strategy

Appendix 3 - Portfolio Maps

Appendix 4 – Top 5 publications in reporting year

Appendix 5 – Recruitment to the NIHR portfolio in the reporting year

Professor Lee Jeys (Sarcoma CSG Chair)

Appendix 1

Membership of the Sarcoma CSG

Name	Specialism	Location
Dr Laura Forker*	Clinical Oncologist	Manchester
Dr Aisha Miah	Clinical Oncologist	London
Dr Beatrice Seddon	Clinical Oncologist	London
Dr Paula Wilson	Clinical Oncologist	Bristol
Dr Alexander Lee*	Clinical Research Fellow	London
Mr Michael Maguire	Consumer	London
Mr Roger Wilson	Consumer	Shropshire
Dr Charlotte Benson	Medical Oncologist	London
Dr Louise Carter	Medical Oncologist	Manchester
Dr Sarah Pratap	Medical Oncologist	Oxford
Dr Sandra Strauss	Medical Oncologist	London
Professor Luc Bidaut	Medical Physicist	Lincoln
Mrs Helen Stradling	Nurse	Oxford
Dr Bernadette Brennan	Paediatric Oncologist	Manchester
Dr Angela Edgar	Paediatric Oncologist	Edinburgh
Dr Malee Fernando	Pathologist	Sheffield
Dr Rajesh Botchu	Radiologist	Radiologist
Professor Sue Burchill	Radiologist	Radiologist
Ms Sarah McDonald	Sarcoma UK Representative	London
Mrs Sharon Forsyth	Senior Trials Coordinator	London
Mr Piers Gaunt	Statistician	Birmingham
Mr Craig Gerrand	Surgeon	Newcastle
Mr Jonathan Gregory	Surgeon	Manchester
Professor Lee Jeys (Chair)	Surgeon	Birmingham

* denotes trainee member

Membership of the Subgroups

Bone Tumour Subgroup		
Name	**Specialism**	**Location**
Dr Fiona Cowie	Clinical Oncologist	Glasgow
Mrs Kelle Vernon	Consumer	Birmingham
Dr Sandra Strauss	Medical Oncologist	London
Professor Jeremy Whelan	Medical Oncologist	London
Dr Bruce Morland	Paediatric Medical Oncologist	Birmingham
Dr Bernadette Brennan	Paediatric Oncologist	Manchester
Professor Donald Salter	Pathologist	Edinburgh
Professor Sue Burchill	Radiologist	Leeds
Mr Matthew Sydes	Statistician	London
Professor Keith Wheatley	Statistician	Birmingham
Mr Craig Gerrand (Chair)	Surgeon	Newcastle

Young Onset Soft tissue Sarcoma Subgroup		
Name	**Specialism**	**Location**
Dr Henry Mandeville	Clinical Oncologist	London
Dr Aisha Miah	Clinical Oncologist	London
Dr Palma Dileo	Medical Oncologist	London
Professor Winette van der Graaf	Medical Oncologist	London
Dr Julia Chisholm	Paediatric Medical Oncologist	London
Dr Maddi Adams**	Paediatric Oncologist	Cardiff
Dr Bernadette Brennan (Chair)	Paediatric Oncologist	Manchester
Dr Merial Jenney	Paediatric Oncologist	Cardiff
Dr Jennifer Turnbull**	Paediatric Registrar	Oxford
Dr Anna Kelsey	Pathologist	Manchester
Dr Kieran McHugh	Radiologist	London
Mr Ross Craigie	Surgeon	Manchester
Mr Tim Rogers	Surgeon	Bristol
Dr Janet Shipley	Translational Scientist	London

* denotes trainee member

**denotes non-core member

Appendix 2

CSG & Subgroup Strategies

A – Main CSG Strategy

Sarcoma CSG Strategy: May 2016 – May 2018

This strategy timeline has been produced to define the Sarcoma Research Strategy Plan and its implementation and will be reviewed and updated at each CSG meeting (NB supported by All)
The document is composed of the following:

Page 2 – 6: NCRI Sarcoma CSG Strategy: plan of implementation, containing agreed strategic objectives (1-6), specific actions, CSG leads and proposed deadlines.

Sarcoma CSG Members		Responsibility
LJ	Lee Jeys	CSG chair
BB	Bernadette Brennan	Young Onset Soft Tissue Sarcoma Subgroup Chair
CG	Craig Gerrand	Bone Sarcoma Subgroup Chair
RB	Ramesh Bulusu	Clinical Oncology
AM	Aisha Miah	Clinical Oncology
BS	Beatrice Seddon	Clinical Oncology
PW	Paula Wilson	Clinical Oncology
MM	Michael Maguire	Consumer representative
RD	Ray Davis	Consumer representative
MF	Malee Fernando	Histopathology
CB	Charlotte Benson	Medical Oncology
HH	Helen Hatcher	Medical Oncology
SP	Sarah Pratap	Medical Oncology
SS	Sandra Strauss	Medical Oncology / NCRAS Chair
JW	Jeremy Whelan	Medical Oncology
JM	Jane Margetts	Medical Oncology
AE	Angela Edgar	Paediatric Oncology / TYA Chair
RBo	Rajesh Botchu	Radiology
RW	Roger Wilson	Sarcoma Charity / Comsumer Representative
SF	Sharon Fortsyth	Trial Co-ordinator
PG	Piers Gaunt	Statistical Lead
JG	Jonathan Gregory	Surgery / SPED CSG
JS	Jonathan Stevenson	Surgery
MW	Mary Wells	Psychosocial CSG
SA	Sam Ahmedzai	Supportive and Palliative Care CSG Chair
DH	Dominque Heymann	Sarcoma Basic Scientist
UV	Ulla Ventham	PA
NK	Nicola Keat	NCRI Exec

Strategic objective	Action	CSG Lead	Date	Outcomes
1a. Portfolio development (general)	Establish a set of priorities for the development and set up of studies that takes account of the NIHR portfolio, international agenda, available funding opportunities and clinical need	ALL	Document key priorities at Strategy Day 5th May 2016 Review Dec 2016	Review Portfolio priorities 6-monthly at CSG meetings
1b. Portfolio development – Advanced disease	Develop a new portfolio study of advanced disease. New study proposed to include all patients with bone and soft tissue sarcoma with a new presentation of metastatic disease. Aim of study is to investigate current treatment with goal to improve quality of life for advanced disease in a longitudinal cohort study with randomisation of local control options, utilising innovative study design . Study to include :- • Supportive care studies with QOL outcomes • Transitional studies with molecular biomarkers • Local control randomisation • Interaction with CRN subspecialty leads • Cross cutting with other CSGs	AM, JW, SS, SA	Identified at Strategy Day 5th May 2016 Progress review 6 monthly at CSG meetings	Working group to develop study / initial feasibility study/ application for programme grant/ leads to fill gaps in portfolio/ leads to engage with other CSGs.
1c. Portfolio development Osteosarcoma	Develop a new portfolio study of osteosarcoma following the hiatus left by a lack of follow up study to EURAMOS. The lack of a new drug has hampered a follow up study, however, many questions remain. Aim of study is recruit all new patients with osteosarcoma in UK. Study to include :- • Molecular biomarkers which predict outcome • Validation of novel classification of surgical margins • Imaging predictors of response to therapy pre-operatively • Randomisation of induction chemotherapy MiniMap vs AB • Interaction with CRN subspecialty leads • Cross cutting with other CSGs • QOL outcomes for patients	BB, SS, AE, SP, RBo, LJ, PG	Identified at Strategy Day 5th May 2016 Progress review 6 monthly at CSG meetings	Working group to develop study / initial feasibility study/ application for programme grant/ leads to fill gaps in portfolio/ leads to engage with other CSGs.
1d. Portfolio development Chondrosarcoma	Develop a new portfolio study of chondrosarcoma. Chondrosarcoma is now most common primary bone sarcoma in UK and has no studies on the portfolio. Aim of study is to recruit all patients presenting to bone sarcoma treating centres with benign or malignant cartilage tumours into longitudinal cohort study with randomisation of local control options for low grade cartilage tumours. Study to include :- • Biobank of cartilage tumours for future research • Investigation of molecular biomarkers (IDH 1 /2 mutation ratio) • Radiological studies of aggressive behaviour (fMRI) • Randomisation local control options for low grade tumours • Ability to include new drugs from on-going Phase 1/11 studies	LJ, JG, JS, CG, Rbo, PG, DH	Identified at Strategy Day 5th May 2016 Progress review 6 monthly at CSG meetings	Working group to develop study from 5 primary bone centres / initial feasibility study with bone sarcoma charity/ application for programme grant/ leads to fill gaps in portfolio/ leads to engage with other CSGs.

Strategic objective	Action	CSG Lead	Date	Outcomes
1e. Portfolio development – Follow up	Develop a new portfolio study to identify optimal methods of follow up of sarcoma patients following treatment, leading to risk stratification and personalised treatment plans. Current methods of post treatment surveillance is variable. Given the large geographic distances travelled to follow up clinics, novel methods of follow up may have benefit. Currently all types of sarcoma are followed up in a similar schedule, risk stratification may allow personalised regimes. Aim of study would be to recruit all new patients with sarcoma in UK to a follow up study. Study to include:- • Molecular & genetic biomarkers of outcome for sarcoma types • PPI involvement of preferences to follow up • Rationalisation of Imaging efficacy in detection of advanced disease • Cost benefit analysis of follow up methods • Novel methods of follow up strategies (distance, nurse led) • QOL outcomes for cancer survivors	JG, BS, CG, MW, RW, RD, MM, PG, FM,	Identified at Strategy Day Day 5th May 2016 Progress review 6 monthly at CSG meetings	Working group to develop study / initial feasibility study/ application for programme grant/ leads to fill gaps in portfolio/ leads to engage with other CSGs.
1f. Portfolio development – Surgical wounds	Continue to develop a surgical study (Whispar) which is a randomised trial of surgical dressings for soft tissue sarcoma wounds. The study randomises between traditional occlusive dressings and topical negative pressure dressings. Initial pilot study has been undertaken winning a prize at the British Sarcoma Group meeting 2016. Aims to recruit patients undergoing surgery for soft tissue sarcomas at units across UK.	JG & WHISPaR study group	Identified at surgical studies meeting 2014 Progress review 6 monthly at CSG meetings	Working group to apply for an RfPB or HTA grant / leads to fill gaps in portfolio
1g. Interaction with international research groups	Identify leads within the CSG to link with the following research groups: EORTC COG euroSARC Conticanet	LJ	May 2016	To keep under review at 6 monthly CSG meeting
1h. Interaction with Cross Cutting groups	Identify leads within the CSG to link with the following cross cutting CSGs and advisory groups: •Primary Care CSG •Biomarker Advisory group •Screening, Prevention and Early Diagnosis (SPED) Advisory Group •CTRAD •Supportive and Palliative Care CSG	LJ	May 2016	To keep under review at 6 monthly CSG meeting

Strategic objective	Action	CSG Lead	Date	Outcomes
1i. National Cancer Registration and Analysis Service (NCRAS)	Establish clear link with Sarcoma Clinical Reference Group Maintain clear links with NCIN the use of data to inform study design and take over long term follow-up	SS / ALL	Report 6 monthly at CSG meeting	NCRAS to have standing item on 6 monthly CSG meetings
2. Key research priority areas	**Surgery** • Increase number of surgical trials within portfolio • Set up a surgical studies subgroup to stimulate research ideas • Local control for chondrosarcoma • Prospective evaluation of surgical margins for osteosarcoma **Osteosarcoma / Chondrosarcoma:** • Establish further trials for these tumour types **Advanced disease :** • Establish further studies for metastatic disease **QOL / Follow up:** • Embed QOL questions into all sarcoma studies • Establish further studies for post treatment surveillance • Embed supportive care studies into future protocols **Translational:** •Work with key clinical and scientific groups to develop embed translational questions into all studies and build translational research platform	LJ JG LJ BB/LJ BB/LJ AM MW JG SA All	May 2016 May 2016 May 2016 May 2016 On-going	Outline proposals to CSG DEC 16 update on progress 6 monthly CSG meeting s
3a. Raising awareness and profile	Regular dissemination of study recruitment activity and outcomes through newsletters, annual meetings and Annual Report and submission of meeting abstracts Communications about new studies with CRN subspecialty leads Engage with sarcoma charities to promote NCRI work during Sarcoma awareness week Have regular NCRI sessions at sarcoma national meetings (BSG, BOOS)	LJ/All UV/All RW/All LJ/All	On-going 2016 2016 On-going	LJ to feedback Participate in future NCRI Subspecialty leads / CSG meetings Discuss next CSG meeting Dec 2016

Strategic objective	Action	CSG Lead	Date	Outcomes
3b. Ensuring successful delivery of studies through integration with NIHR CRN: Cancer	• CSG members to commit to delivering studies developed by the CSG • Interaction with LCRN Subspecialty Leads to determine placement of new studies and address barriers to actively recruiting patients • Monitor recruitment to portfolio studies, esp those developed by the CSG to ensure delivery to time and target • Contribute as far as possible to NIHR CRN: Cancer Speciality Objectives so they reflect what LCRNs need to deliver to ensure lung cancer patients can access the full portfolio of studies within UK	ALL ALL ALL ALL	On-going On-going On-going On-going	Recruit CSG-led studies to time and target Good regional placement of studies Meet NIHR CRN Speciality Objectives
3c. Maximise output from clinical trials	• Establish working groups for new studies within 6 weeks of funding award to facilitate swift set up, including representation from CI, CRCTU, NIHR CRN: Cancer • Ensure Translational, QOL & supportive questions embedded into all studies opened • Design studies which aim to recruit as many sarcoma patients as possible by asking multiple questions within same study	CI/CTUs All All	On-going	Update at six monthly CSG meetings
4. Strengthen UK wide and international working	Refine prioritisation process for international clinical trials to be submitted for funding to optimise the timing and success of applications Identify UK selling points for sarcoma research to identify and promote the flagships studies on the portfolio Work to badge academically sponsored NCRI CSG studies as 'NCRI study into x' Work to ensure research remains core to NHS service and is recognised in all job plans .	All All All	On-going On-going May 2016 May 2016	Update at six monthly CSG meetings

Strategic objective	Action	CSG Lead	Date	Outcomes
5. CSG structure and function	Establish Surgical Studies subgroup	JG/CG/LJ	May 2016	Establish appropriate representation at CSG meetings to foster research ideas and new studies Diversify portfolio studies to include areas of unmet need
	Working Party for new study proposals from strategy day	LJ/JG/BB/AM	May 2016	
	Diversify membership of CSG to include Basic scientist, Psychosocial, Specialist nursing experience in membership to reflect need for portfolio studies in these areas.	LJ/NK	May 2016	
	Regular invitation to attend CSG from other relevant CSGs, NCRAS and Advisory Groups depending on agenda items & proposals	LJ/NK/UV	May 2016	
	Identify mentors for future trainee registrars in the CSG / subgroups	LJ	May 2016	
	Identify mentors for new PPI members in CSG / subgroups	LJ	May 2016	
6. Patient and Public Involvement and Impact	Ensure consumers remain associated with the development of every new study at an early stage	All	On-going	Ensure studies have relevance to consumers through CSG meeting / reports
	Consider developing research studies to address key questions of concern to PPI representatives and other consumers	MM/RD to bring questions to the group	On-going	

B – Bone Tumour Subgroup Strategy

Strategic priorities

1. To develop and deliver a study in chondrosarcoma.
2. To develop and deliver a study in osteosarcoma.
3. To support the delivery of studies in Ewings sarcoma.
4. To promote national collaboration in the development and delivery of studies.

Progress against priorities

1. A study of IDH1/2 mutations in the serum of chondrosarcoma patients has been funded and will open this year.
2. A proposal for funding of a large umbrella study in osteosarcoma is being developed with a view to a submission to BCRT later this year.
3. Recruitment to EE2012, REECUR and related studies has been supported by the Subgroup. Adoption to the portfolio has increased the opportunity to recruit to the GenoEwings and Predict studies.
4. The Subgroup is able to engage with a larger number of members increasing its national reach thanks to BCRT funding. All studies under development are either multicentre or will become so, including the chondrosarcoma study, the osteosarcoma study in development and the Sarcoma PROMS study.

C – Young Onset Soft-tissue Sarcoma Subgroup Strategy

The group recognises the continuing challenges:

• To increase participation of the TYA population in trials, indeed extending all our trials and research to the adult age group.

• The necessity for stable international consortia to develop trials where patient numbers in the UK are small.

• Obtaining access to new agents from pharma companies for younger patients, and indeed in sarcomas.

• Funding the parallel biological studies in international trials

Agreed strategic priorities for YOSS:

1. To open a first line study in Rhabdomyosarcoma across all ages in paediatric, TYA and adult sites in UK and indeed European countries who are part of the EpSSG

2. To build on current relapse studies in RMS using VIT as backbone- this strategic aim is incorporated into the FaR-RMS study

3. To develop an all age European study in specific soft tissue which occur in paediatric, TYA and adult age group e.g. Synovial Sarcoma, MPNST, leiomyosarcoma and liposarcoma.

4. To build on the outcomes of other rare sarcomas from the NRSTS study to develop further clinical trials specifically Rhabdoid tumours at all anatomical sites.

5. To embed biological studies, biomarkers and novel targets into clinical trial portfolio

6. To open a prospective cohort study with a biological question that may be useful for all the NRSTS subtypes in particular those which mainly occur in the paediatric age group.

7. To increase the TYA population in sarcoma studies.

Planned implementation:

1. FaR-RMS: A multiarm-multistage study for children and adults with localised and metastatic Frontline and Relapsed RhabdoMyoSarcoma new study proposal has been funded by CRUK and will be opened by the end of 2018.

2. See above

3. To develop an all age European study in specific soft tissue sarcomas. There is a trial in early development within Europe to examine the role of Olaratumab in addition to ifosfamide and doxorubicin in high risk soft tissue sarcomas, which will lower the traditional age limit of 18 to include TYA and paediatric subjects.

4. To build on the outcomes of other rare sarcomas from the NRSTS study to develop further clinical trials (EURO RHABDOID 2017 study in planning).

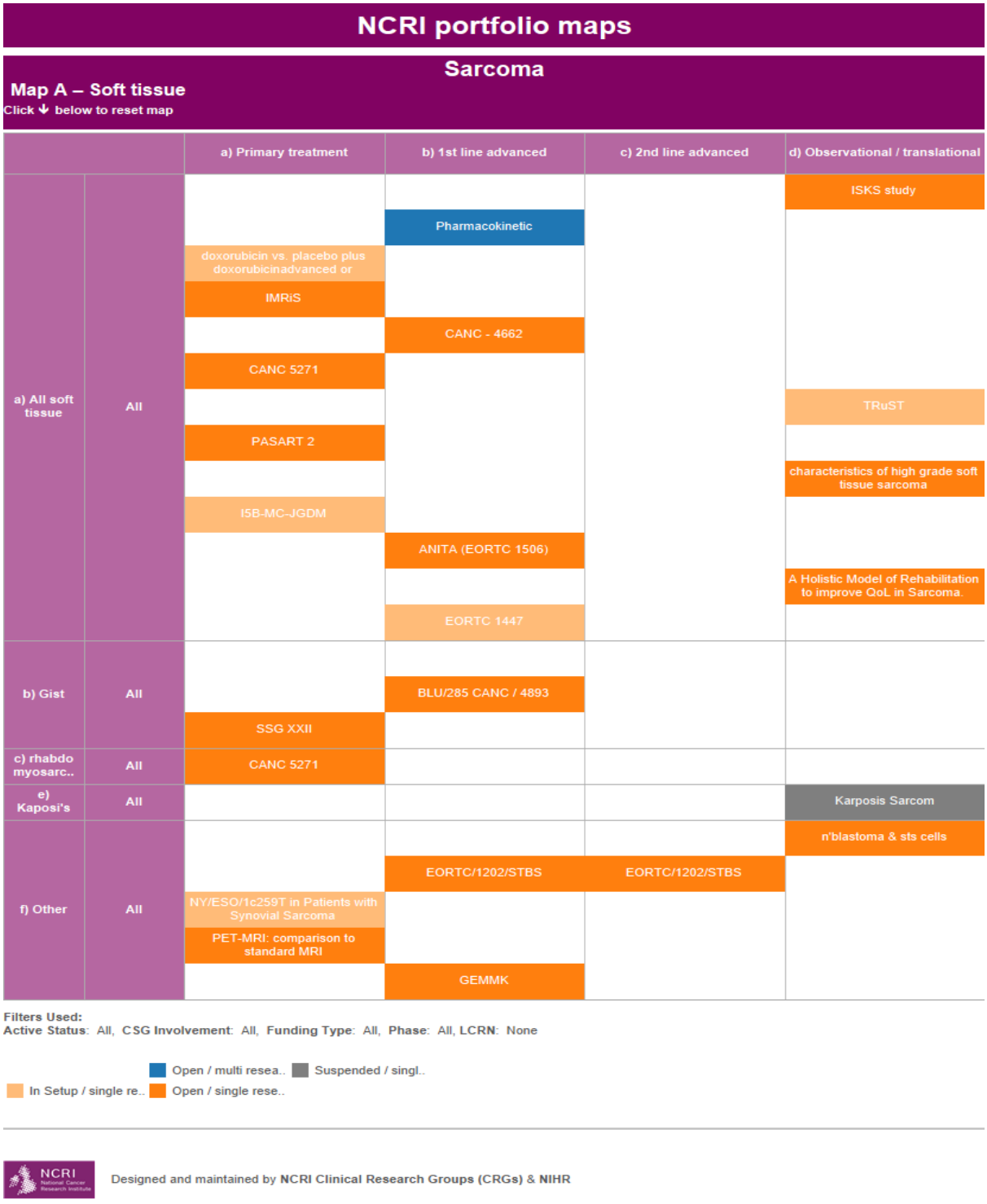
5. To embed biological studies, biomarkers and novel targets into clinical trial portfolio. This will be achieved in FaR-RMS and EpSSG NRSTS 2018

6. To open a prospective cohort study with a biological question that may be useful for all the NRSTS subtypes. This will be achieved with EpSSG NRSTS 2018.

7. To increase the TYA population in sarcoma studies- this will be achieved by extending the upper age range for study entry

Appendix 3

Portfolio maps

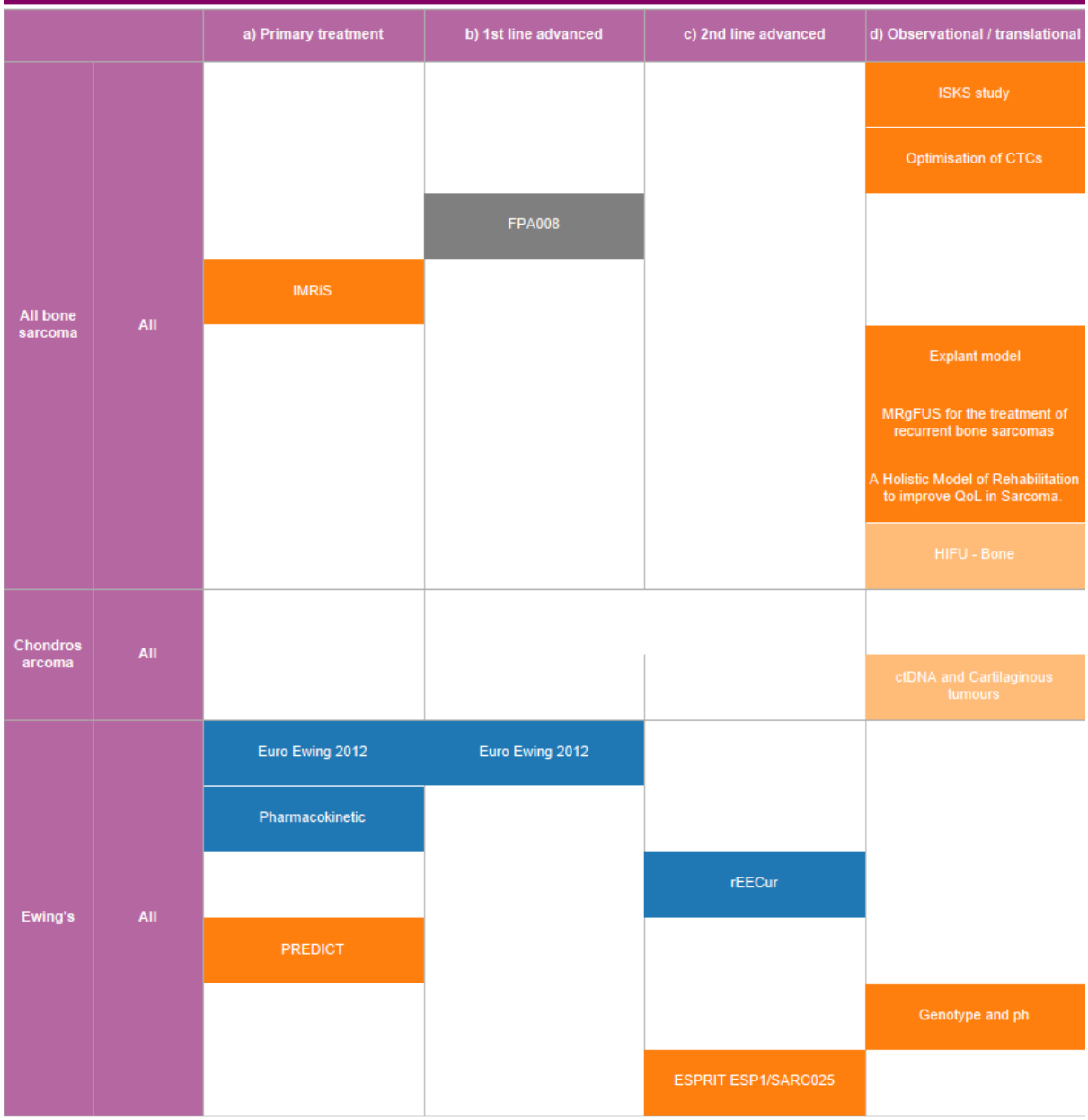


NCRI portfolio maps

Sarcoma

Map B – Bone

Click ↓ below to reset map



Filters Used:
Active Status: All, **CSG Involvement**: All, **Funding Type**: All, **Phase**: All, **LCRN**: None

Open / multi resea.. Suspended / singl..
In Setup / single re.. Open / single rese..

NCRI National Cancer Research Institute

Designed and maintained by **NCRI Clinical Research Groups (CRGs)** & **NIHR**

Appendix 4

Top 5 publications in the reporting year

Please note that the below is incomplete

Trial name & publication reference	Impact of the trial	CSG involvement in the trial
1. Survival is influenced by approaches to local treatment of Ewing sarcoma within an international randomised controlled trial: analysis of EICESS-92. Whelan J et al, Clin Sarcoma Res. 2018 Mar 30;8:6.	Unexpected differences in EFS and OS occurred between two patient cohorts recruited within an international randomised trial. Failure to select or deliver appropriate local treatment modalities for Ewing's sarcoma may compromise chances of cure. 5-year EFS rates were 43% (95% CI 36-50%) and 57% (95% CI 52-62) in the CCLG and GPOH patients, respectively; corresponding 5-year OS rates were 52% (95% CI 45-59%) and 66% (95% CI 61-71). CCLG patients were less likely to have both surgery and radiotherapy (18 vs. 59%), and more likely to have a single local therapy modality compared to the GPOH patients (72 vs. 35%). Forty-five percent of GPOH patients had pre-operative radiotherapy compared to 3% of CCLG patients. In the CCLG group local recurrence (either with or without metastases) was the first event in 22% of patients compared with 7% in the GPOH group	Members of the CSG were involved in the development of the EICESS-92 study and wrote this paper from the data.
2. Surgery alone is sufficient therapy for children and adolescents with low-risk synovial sarcoma: a joint analysis from the European paediatric Soft tissue sarcoma Study Group	It confirms in large numbers that this should be the standard therapy for these patients, and small tumours do not need adjuvant chemotherapy	Members of the CSG were involved in the development of the EpSSG NRSTS study and co- wrote this paper from the data.

and the Children's Oncology Group. Ferrari A et al, Eur J Cancer 2017 Jun;78:1-6.		
3. Alveolar soft part sarcoma in children and adolescents: The European Paediatric Soft Tissue Sarcoma study group prospective trial (EpSSG NRSTS 2005). Brennan B et al, Pediatr Blood Cancer. 2018 Apr;65(4).	This report demonstrates the ability to run prospective pediatric studies in NRSTS in multiple European countries, despite the small numbers of ASPS patients. We can conclude that for the majority with small resected tumors, there were few events and no deaths.	Members of the CSG were involved in the development of the EpSSG NRSTS study and co- wrote this paper from the data.

Appendix 5

Recruitment to the NIHR portfolio in the reporting year

In the Sarcoma CSG portfolio, 6 trials closed to recruitment and 11 opened.

Summary of patient recruitment by Interventional/Non-interventional

Year	All participants		Cancer patients only		% of cancer patients relative to incidence	
	Non-interventional	Interventional	Non-interventional	Interventional	Non-interventional	Interventional
2013/2014	43	195	25	195	-	-
2014/2015	145	115	145	115	-	-
2015/2016	58	130	58	130	-	-
2016/2017	208	206	184	206	-	-
2017/2018	360	223	346	223	-	-