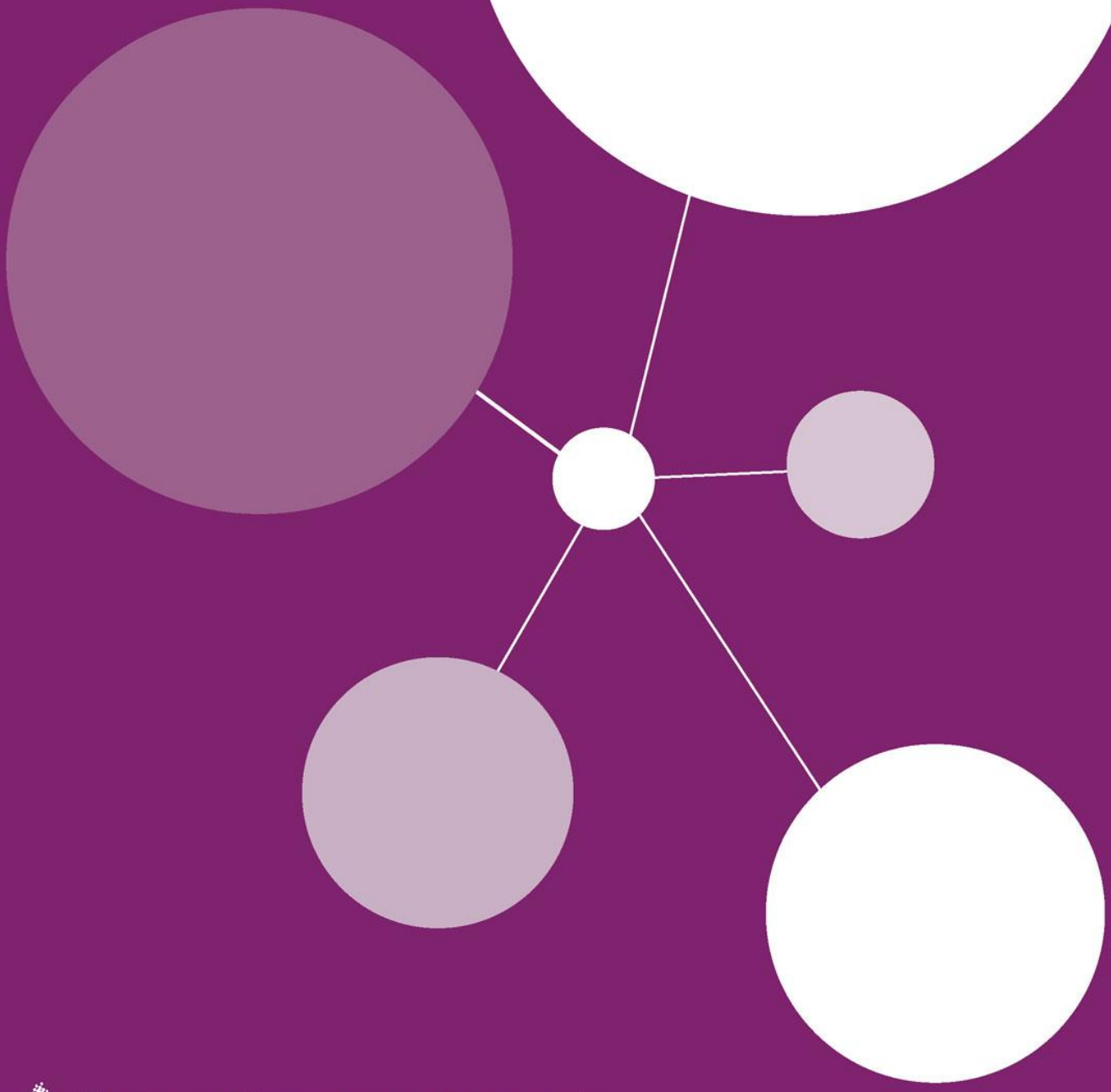
NCRI
National
Cancer
Research
Institute

NCRI Sarcoma Clinical Studies Group

Annual Report 2016-17



Partners in cancer research

NCRI Sarcoma CSG Annual Report 2016-17

1. Executive Summary (including top 3 achievements in the year)

The main aim of the CSG remains to increase the number of studies open to patients with sarcoma in the UK, with the ultimate goal of having a study to which any patient with sarcoma in the UK can contribute and the Group continues to develop broader studies to meet this aim. The CSG has focused on developing both disease specific studies but also studies on other aspects of sarcoma, such as quality of life studies.

The availability of funding for rare cancer and non-interventional studies, particularly for patient related outcomes, remains a challenge for the CSG. The Group proactively invited representatives of major NIHR adopted funders such as Cancer Research UK, Bone Cancer Research Trust and Sarcoma UK to meetings to better understand funding opportunities and focus research ideas. The CSG also acknowledges the need for further engagement with CRN Sarcoma Subspecialty Leads (SSLs) and is creating an annual meeting between the groups to coordinate trial development and delivery.

The three main achievements of the CSG this year were:

1. Doubling the number of sarcoma patients recruited to all study types compared to 2015-16 and having the most patients recruited to non-interventional studies and second most patients recruited interventional studies on the portfolio in the last five years. This has been in the context of only one major international bone sarcoma study open and 26 new studies opening in 2016-17.
2. Funding and adoption of the first chondrosarcoma study on the portfolio. This is an exciting study which will explore both clinical outcomes and translational basic science which was formulated as a direct response from ideas from the Sarcoma CSG strategy away day and was funded within 12 months of conception.
3. Further development of osteosarcoma and follow-up studies generated at the Sarcoma CSG strategy away day which are close to submission for funding.

2. Structure of the Group

The Group acknowledged the massive to contribution to sarcoma research by Professor Jeremy Whelan and was thankful to the work of Mr Jonathon Stevenson, both of which rotated off the main CSG this year but continue to be members of the Bone Tumour Subgroup.

The CSG welcomed Dr Alexander Lee (trainee in medical oncology, completing a PhD on the immunological aspects of sarcomas at the Institute of Cancer Research) and Dr Laura Forker (trainee in clinical oncology and PhD clinical fellowship in soft tissue sarcoma molecular biology funded by Cancer Research UK) as trainee representatives.

The CSG has recently advertised for new members and depending on applications, expertise in basic science sarcoma research is anticipated.

3. CSG & Subgroup strategies

Main CSG

The main focus of the CSG remains to increase the number of trials available for sarcoma patients in the UK. The Group strategy is to develop new trials with both interventional and non-interventional arms, with the aim of allowing as many patients as possible with sarcoma to enter data into studies. The CSG is interested in novel methods, such as Bayesian statistics, which allow patients not participating in interventional arms to contribute data to the study priors. Interventional disease specific trials remain important to the Group and portfolio; however, in a rare disease type, information from large patient groups with a variety of disease subtypes would be invaluable, particularly in quality of life, follow-up and metastatic studies. There have been representatives of major NIHR research funders at CSG meetings to allow better understanding of funding opportunities with relevance to sarcoma. The CSG strategy away day also had representation from the successful Tracer-X study to give insight into the successes and difficulties of running large multi-arm studies.

The aim to increase studies in bone sarcomas in the CSG 2016-18 strategy document (see Appendix 2; 1c and 1d) has shown significant progress. A study in chondrosarcoma entitled "Does circulating DNA predict the grade and disease burden of chondrosarcoma? A nationwide collaboration for primary bone tumour research" has been funded and will be opened shortly. This is the first national collaborative study funded in this disease type. Progress has also been made in the proposed osteosarcoma study, with a view to submitting funding applications shortly. Slower but steady progress in the follow-up and metastatic studies are being made and are under review by the Group.

Progress has been made on collaboration with the NIHR Cancer: CRN Sarcoma SSLs, with action to hold an annual combined meeting plus SSLs have been invited to attend CSG meetings to further foster collaboration and delivery of portfolio trials.

Bone Tumour Subgroup (Chair, Mr Craig Gerrand)

The strategic approach of the Bone Tumour Subgroup this year has been to develop studies in bone sarcoma through wide engagement, including involvement with charitable partners and national collaboration. Our aim has been to develop studies where there were none, in particular for osteosarcoma and chondrosarcoma, to ensure that learning around protocols in one study are made available for others and that studies are opened in as many centres as feasible. For example, a study of serum mutations in patients with chondrosarcoma has been developed by the Subgroup and funded by BCRT, filling a significant gap in the portfolio.

The Subgroup continues to be supported by BCRT for which we are very grateful and the portfolio for bone sarcoma studies has expanded over the last year. Studies in Ewings sarcoma include: Euro Ewings 2012, which continues to recruit patients across Europe and includes a translational

arm; the PREDICT study of surgical margins, now open nationally; GenoEWING study of drug resistance; REECUR for relapsed patients and a pharmacokinetic study of Ewings patients.
In osteosarcoma, a pilot study of circulating tumour cells has completed recruitment and remains a good example of national sharing of biospecimens. There is a phase II/III study of lenvatinib for relapsed malignancies which is now open in Newcastle and an fMRI study in Birmingham which is still recruiting slowly. Plans for an umbrella study are progressing with the aim of recruiting all patients with an osteosarcoma. A revised version will be submitted to funders this year and there is an allied large bequest to support associated biological studies. A plan for a chordoma registry is in development.

Young Onset Soft-tissue Sarcoma (YOSS) Subgroup (Chair, Dr Bernadette Brennan)

The YOSS Subgroup has continued to be very successful in 2016-17. The rhabdomyosarcoma (RMS), RMS 20015 study closed in December 2016, having completed two randomisations efficiently using the cohort of rare patients for both an up front, and for many, a second randomisation. The successor study FaR-RMS: A multiarm-multistage study for children and adults with localised and metastatic rhabdomyosarcoma, is awaiting a decision if it will be funded by CRUK.

In non-rhabdomyosarcoma soft tissue sarcomas (NRSTS), EpSSG NRSTS 2005 closed in December 2016. Currently the cohort of desmoid tumours, malignant peripheral nerve sheath tumours, epithelioid sarcomas, and alveolar soft part sarcomas have been presented at international meetings and for some a paper is ready to be submitted for publication. Furthermore, data already published such as the synovial sarcoma cohort have been combined with the USA COG group's data for a further publication this year. The next successor studies for either the whole cohort of NRSTS, or specific tumour types such as synovial sarcoma and malignant rhabdoid tumours are already in development.

Trials in development are:

- EUROJOSS study: This study aims to set up the first all age trial in Europe for synovial sarcoma.
- EURO RHABDOID 2017: This study hopes to add a new agent, targeting the epigenetic pathway in rhabdoid tumours alongside the established backbone from the EpSSG study.
- EpSSG NRSTS 2018: As a successor to EpSSG NRSTS 2005, we are proposing this study which will be a prospective cohort study with a biological question.

The Subgroup recognises the continuing challenges:

- To increase participation of the TYA population in trials and 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.

4. Task groups/Working parties

Gynaecological Sarcoma Working Party

This Working Party (WP) was set up in 2011 to develop trials and improve outcomes for this long-

neglected patient group. Dr Benson has taken over as Chair of the WP and a trial is in development with the Royal Marsden Hospital. There are currently two Gynaecological Sarcoma EORTC studies open in the UK.

Lung Metastases Task Group

This is a new Task Group (TG) chaired by Dr Aisha Miah. A trial is being developed investigating metastatic disease at first presentation, involving a prospective evaluation of various quality of life areas and will include tissue collection. The aim is to reduce clinical uncertainty of treatment of these patients where there is no evidence base and to improve PROMs. HN5000 was noted as a good example and will be used as a model for this study. The study is in preparation for a funding application and anticipates a large number of recruits amongst all sarcoma types.

5. Patient recruitment summary for last 5 years

This has been an excellent year for increasing both the number of studies of sarcoma on the portfolio and numbers of patients recruited to studies. In the Sarcoma CSG portfolio, six trials closed to recruitment and 7 new studies opened. The CSG has seen a doubling of the number of sarcoma patients recruited to all study types compared to 2015-16 and has the most patients recruited to non-interventional studies and second most patients recruited interventional studies on the portfolio in the last five years. Close collaboration from NIHR funder partners, meaning studies can be adopted onto the portfolio, has been partly responsible for this and has led to a greater number of studies funded and being adopted to the portfolio this reporting year.

Table 1 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
2012/2013	194	272	151	272	4.7	7.8
2013/2014	43	195	25	195	-	-
2014/2015	145	115	145	115	-	-
2015/2016	58	130	58	130	-	-
2016/2017	208	206	184	206	-	-

6. Links to other CSGs, international groups and network subspecialty leads

Following the Chairs' Forum and strategy day, the CSG has had cross fertilisation with the Consumer Forum, SPED Advisory Group, Psychosocial Oncology & Survivorship CSG, Supportive & Palliative Care CSG, Primary Care CSG and Teenage & Young Adult (TYA) and Germ Cell Tumours (GCT) CSG. Several members of the Group also sit on other CSGs and Dr Sandra Strauss, the SSCRG chair for NCRAS for sarcoma, also sits on the CSG.

Links with the SSLs remains an important partnership to the CSG. Currently there are significant unfilled SSL positions for sarcoma and the CSG is committed to fostering closer links to ensure recruitment to available trials is at a maximum. Telephone conferences have taken place in an attempt to improve the communication between the CSG and SSLs and an annual meeting is being convened to share information and encourage collaboration.

Dr Charlotte Benson continues to be involved with the EORTC and Dr Sandra Strauss provides a link with the USA Sarcoma Alliance for Research through Collaboration (SARC). Close collaborations are also maintained with EOI, SIOP and COSS through Professor Jeremy Whelan and Dr Bernadette Brennan. We are developing collaboration with the Scandinavian Sarcoma Group to open their GIST trial in the UK.

7. Funding applications in last year

The YOSS Subgroup have a full application pending decision currently with CRUK. A number of sarcoma charities are NIHR Partners and through working with them, particularly with Sarcoma UK, the CSG has increased the number of projects securing funding and subsequently being adopted onto the portfolio. A number of pilot or feasibility projects are being funded prior to larger CRUK applications.

Table 2 Funding submissions in the reporting year

Cancer Research UK Clinical Research Committee (CRUK CRC)			
Study	**Application type**	**CI**	**Outcome**
May 2016			
MiRNA expression in plasma, tumour tissue and stem cells, a tool for measuring the effectiveness of chemotherapy in osteosarcoma	Full application	Professor Gordon Blunn	Not funded
A multiarm-multistage study for children and adults with localised and metastatic Frontline and Relapsed RhabdoMyoSarcoma	Outline application	Dr Meriel Jenney, Dr J Hans Merks, Dr Julia Chisholm & Professor Keith Wheatley	Full application invited
November 2016			
METRONOME: a randomised placebo-controlled phase II clinical trial of maintenance metronomic oral cyclophosphamide following induction chemotherapy for advanced soft tissue sarcoma	Outline application	Dr Robin Young	Not invited to full
Other committees			
Study	**Committee & application type**	**CI**	**Outcome**
Development of a sarcoma-specific patient reported outcome measure	Sarcoma UK	Rachel Taylor, Lindsey Bennister, Mary Wells, Lorna Fern, Craig Gerrand, Lesley Storey, Julie Woodford, Rachel Windsor, Jeremy Whelan	Funded
Can a holistic model of rehabilitation improve quality of life after treatment for lower extremity sarcoma? A pilot and feasibility study.	Sarcoma UK	Craig Gerrand, Sherron Furtado, Lynn Rochester	Funded
Does PET-MRI of myxofibrosarcoma improve the local staging of disease compared with standard MRI?	Sarcoma UK	George Petrides, Craig Gerrand, Simon Lowes, Ross Maxwell	Funded

8. Collaborative partnership studies with industry

Four academic studies are partnerships with Industry: MEMOS (Takeda), LINES (Astellas), CASPS (AstraZeneca), and SCART (AstraZeneca). All four are open and recruiting. These trials address rare tumour types that would not otherwise have attracted the attention of Pharma. During the process of trial design for several new studies under development in the CSG, there have been ongoing discussions with several Pharma companies to investigate opportunities with novel agents suitable for sarcoma studies.

9. Impact of CSG activities

Our publications are testament to the high impact of our clinical research (see Appendix 4). The routine management of bone and soft tissue sarcomas has been guided by NCRI supported trials. Ultimately, our trials are practice-changing when they lead to new drugs being licensed (e.g. pazopanib for STS) or inform NICE, ESMO and ASCO practice guidelines. We anticipate that our NCRI-led trials, VORTEX and GeDDiS, will have such impact having been presented recently at international meetings; however, full publications are yet to be available. In particular, the EORTC trials 62931 and 62012 are the foundation of STS management in the UK and Europe. 62931 confirmed that adjuvant chemotherapy offers no survival advantage over observation alone in resected high-risk soft tissue sarcoma.

A multitude of emerging results from EuroEwings 99 have had practice changing effect of the treatment of this disease. Results of post-operative radiotherapy from EE99 study have showed marked reduction in the local recurrence of Ewings, with a trend to improvement in overall survival, will change practice worldwide for this rare type of tumour. Recently presented data from EE99 showed that combined therapy (chemotherapy, surgery and radiotherapy) had both a local control and survival advantage over either dual modality therapy. These results have dramatically altered of treatment with pelvic Ewings in the UK.

The published EURAMOS-1 results do not support the addition of ifosfamide and etoposide to postoperative chemotherapy in patients with poorly responding osteosarcoma because its administration was associated with increased toxicity without improving event-free survival. The results define standard of care for this population and add to the previously published results from this study.

In paediatric sarcoma, trial results from EpSSG NRSTS 2005 proved that conservative therapy is possible in infantile fibrosarcoma as only three children required mutilating surgery and alkylating or anthracycline based chemotherapy was avoided in 71% of patients needing chemotherapy. These results will improve the life of children with sarcoma worldwide. The CSG has continued to engage with NICE appraising new drugs efficacy and NIHR funders on sarcoma related projects.

The CSG has continued to engage with NICE appraising new drugs efficacy (Olaratumab in combination with doxorubicin for treating advanced soft tissue sarcoma) and NIHR funders on sarcoma related projects (Clinical Research Committee for CRUK).

10. Consumer involvement

Ray Davies and Michael Maguire continue as the consumer representatives on the CSG, with the vastly experienced patient advocate Roger Wilson CBE continuing to support consumer involvement and the patient perspective on the Group. They do so by contributing to discussions at meetings, reporting relevant feedback, news and information on events from the wider consumer community and events they have attended that may support the work of the CSG.

Following the Sarcoma CSG strategy day in 2016, Roger, Ray and Michael have continued to contribute to the development of a potential clinical study using mobile/app technology. They are currently working with Dr Paula Wilson on the first part of a planned three-part research project in follow-up.

They remain an integral part of the CSG and our plan to increase the value of consumer involvement in the work of the Sarcoma CSG, with them lending their consumer perspective to developing study ideas. In the design of a new surgical wound site study, 35 consumer surveys were very revealing about consumers' feelings regarding wounds. There have been three meetings at different sites to get consumer data.

11. Open meetings/annual trials days/strategy days

The strategy days last year were extremely productive for the Group. One study design idea from the day, was successful in obtaining funding from Bone Sarcoma Research Trust and aims to join the portfolio and commence recruitment later in 2017. This will be the first Chondrosarcoma study on the portfolio and ensures collaboration from the five bone sarcoma MDTs with England. Another project on Osteosarcoma was submitted for a feasibility grant and, following feedback, is being submitted shortly for funding along with two other studies being prepared for funding submission.

12. Priorities and challenges for the forthcoming year

The top three priorities of the sarcoma CSG in 2017-18 are:

1. To build on the excellent work emanating from the strategy day in 2016: One study idea has led to successful funding from a charity allied to sarcoma research; however, an initial funding application for one of the study ideas was initially unsuccessful despite positive feedback and a further refined application is planned. The whole CSG remains supportive and committed to helping the lead investigators to develop the initial ideas for studies in Osteosarcoma, patient follow-up and metastatic sarcoma to ensure successful funding for these projects is achieved.
2. To develop new studies ideas in areas of unmet need within the Sarcoma CSG portfolio: The two main areas are broad studies into soft tissue sarcomas (STS) and surgical studies. The study ideas into patient follow-up and metastatic sarcoma will go in some part to delivering studies in this area, together with a new study into sarcoma patient related outcome measures, recently added to the portfolio. However, as the largest disease subtype within our CSG, studies into STSs remain under-represented. The CSG will strive to develop new broader studies aimed at recruiting as many patients with sarcoma as possible. Currently, there are approximately 2,000 new sarcoma diagnoses

per year within the UK and in 2016-17,390 patients were recruited to trials, leaving significant room for improvement.

3. To diversify the membership of the Sarcoma CSG: The main CSG is currently made up of eight adult oncologists, three surgeons, two paediatric oncologists, two consumer representatives, two trial experts, a histopathologist, a sarcoma specialist nurse, a researcher and a radiologist. At the last CSG meeting it was felt that recruitment of further basic science experts and pathology experts would be desirable to enhance the breadth of specialty experience within the Group membership. The CSG plans to invite representation from other CSGs, in particular the Primary Care and Psychosocial Oncology & Survival CSGs, to help develop study ideas, as well as using the SPED and Imaging Advisory Groups for support. The Biomarker and Proton Beam groups are of particular interest and would lend valuable expertise to forthcoming study designs. The rotational nature of membership will that mean vacancies on the CSG will allow applications from the sarcoma community and these will be particularly encouraged from areas that are underrepresented.

The CSG feels the main challenges to the Group for 2016-17 remain similar to previous years. In particular, these are:

1. To obtain national funding for innovative trial designs for the projects proposed from the strategy day: National funders have recently funded trials of innovative design and adding "value for money" by answering several questions (including biological questions) and may help applications to be more successful. However, this remains a great challenge, especially for a rare cancer type. The engagement of NIHR adopted charities particularly focused on sarcoma, such as Sarcoma UK, has recently managed to guarantee applicants for grants are supported and encouraged to ensure funded projects are adopted on to the portfolio. The CSG also encourages all projects related to sarcoma to be presented at CSG meetings prior to funding application in an attempt to improve and support the application, hence, increase the likelihood of successful funding. The CSG will work with other NIHR sarcoma charities to encourage funded projects are adopted onto the portfolio.
2. Recruitment to and management of existing portfolio studies will rely more heavily on NIHR Cancer: CRN Subspecialty Leads and their engagement to the studies will be important. This will also have major significance when launching new studies and the enthusiasm and cooperation of CSG members will be paramount in ensuring their success. Fortunately, with a limited number of treating centres for sarcoma, the Group and sarcoma community can levy influence on these centres. Engagement with the SSLs has been limited in 2016-17 and a significant number of these posts remain unfilled in sarcoma. The CSG Chair will continue to engage with the networks and further face-to-face meetings and telephone conferences have been arranged to increase the working relationship of the CSG and SSLs. The CSG recognizes the mutual benefit this relationship will bring to both study design and delivery.
3. To encourage participation of clinicians, researchers, nurse and Sarcoma MDTs to participate in Sarcoma research: In a super-specialised field of medicine where there are a limited number of regional MDTs (13 STS, five bone) within England and Wales, it is important that each MDT actively encourages participation in research and recruitment to trials. Encouraging new researchers to submit ideas or apply for membership of the CSG is challenging when there is a limited number of centres involved in sarcoma research. The Group continues to give representation to charities and national sarcoma meetings.

However, the CSG plans to engage more locally with regional MDTs and research institutions to raise the profile of the CSG, explain our role in national research, support researchers with study ideas in sarcoma and encourage them to share these with the CSG to allow us to develop these with the researcher in an attempt to increase the number of trials on the portfolio.

13. 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 (YOSS) Subgroup Strategy

Appendix 3 - Portfolio Maps

Appendix 4 - Publications in previous year

Appendix 5 - Major international presentations in previous 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	Essex
Miss Ray Davis	Consumer	Bingley
Dr Malee Fernando	Histopathologist	Sheffield
Dr Charlotte Benson	Medical Oncologist	London
Dr Helen Hatcher	Medical Oncologist	Cambridge
Dr Sarah Pratap	Medical Oncologist	Oxford
Dr Sandra Strauss	Medical Oncologist	London
Mrs Helen Stradling	Nurse	Oxford
Dr Sarah McDonald	Observer: Sarcoma UK	London
Dr Bernadette Brennan	Paediatric Oncologist	Manchester
Dr Angela Edgar	Paediatric Oncologist	Edinburgh
Dr Rajesh Botchu	Radiologist	Kettering
Mr Roger Wilson	Sarcoma UK	Shropshire
Mrs Sharon Forsyth	Senior Trials Coordinator	London
Dr 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**
Professor Susan Burchill	Cancer Biologist	Leeds
Dr Fiona Cowie	Clinical Oncologist	Glasgow
Mrs Kellie Vernon	Consumer	Birmingham
Dr Sandra Strauss	Medical Oncologist	London
Professor Jeremy Whelan	Medical Oncologist	London
Professor Donald Salter	Pathologist	Edinburgh
Dr Bernadette Brennan	Paediatric Oncologist	Manchester
Professor Susan Burchill	Paediatric Oncologist	Leeds
Dr Bruce Morland	Paediatric Oncologist	Birmingham
Mr Matthew Sydes	Statistician	London
Professor Keith Wheatley	Statistician	Birmingham
Mr Craig Gerrand (Chair)	Surgeon	Newcastle
Professor Robert Grimer	Surgeon	Birmingham
Mr Jonathan Stevenson	Surgeon	Shropshire

Young Onset Soft tissue Sarcoma (YOSS) Subgroup		
Name	**Specialism**	**Location**
Dr Henry Mandeville	Clinical Oncologist	Sutton
Dr Aisha Miah	Clinical Oncologist	London
Dr Anna Kelsey	Histopathologist	Manchester
Dr Palma Dileo	Medical Oncologist	London
Dr Madeleine Adams**	Paediatric Oncologist	Cardiff
Dr Jennifer Turnbull*	Paediatric Registrar	Oxford
Dr Bernadette Brennan (Chair)	Paediatric Oncologist	Manchester
Dr Julia Chisholm	Paediatric Oncologist	London
Professor Winette van der Graaf	Professor of Personalised Oncology	London
Dr Kieran McHugh	Radiologist	London
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 (YOSS) Subgroup Strategy

Strategic priorities

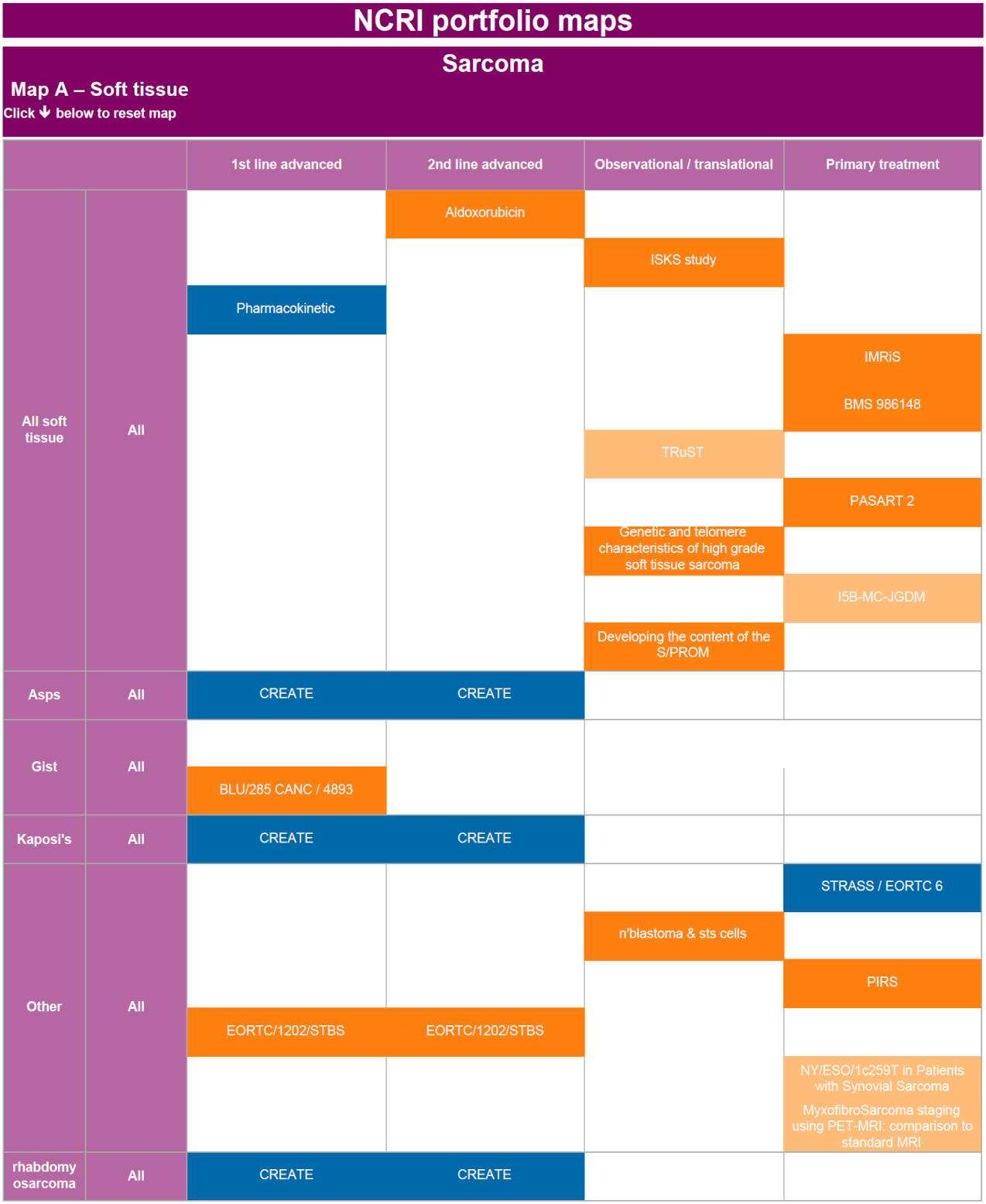
1. To open a first line study in Rhabdomyosarcoma across all ages.
2. To build on current relapse studies in RMS using VIT as the backbone.
3. To develop an all age European study in Synovial Sarcoma.
4. To build on the outcomes of other rare sarcomas from the NRSTS study to develop further clinical trials, specifically Rhabdoid tumours at all sites and synovial sarcoma.
5. To embed biological studies, biomarkers and novel targets into the clinical trials portfolio.
6. To open a prospective cohort study with a biological question that may be useful for all the NRSTS subtypes.
7. To increase the TYA population in sarcoma studies.

Planned implementation

1. and 2. FaR-RMS: A multiarm-multistage study for children and adults with localised and metastatic Frontline and Relapsed RhabdoMyoSarcoma – a new study proposal has been submitted for funding to CRUK for funding and the outcome will be known soon (*Post note* this study has been supported by CRUK since the end of the reporting year).
3. To develop an all age European study in Synovial Sarcoma - planned EUROJOSS study.
4. To build on the outcomes of other rare sarcomas from the NRSTS study to develop further clinical trials - EURO RHABDOID 2017 and EUROJOSS study planned.
5. To embed biological studies, biomarkers and novel targets into the clinical trials 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

		1st line advanced	2nd line advanced	Observational / translational	Primary treatment
All bone sarcoma	All	FPA008		CREATE ISKS study Optimisation of CTCs Explant model MRgFUS for the treatment of recurrent bone sarcomas Developing the content of the S/PROM	IMRiS IDRIS
Chondrosarcoma	All				
Ewing's	All	Euro Ewing 2012 rEECur	ESPRIT ESP1/SARC025	Genotype and ph	Euro Ewing 2012 Pharmacokinetic rEECur PREDICT

Filters Used:
Active Status: All, **CSG Involvement**: All, **Funding Type**: All, **Phase**: All

Open Multi CSG
Open Single CSG
Null
In Setup, Waiting ..
Suspended Single..

Appendix 4

Publications in the reporting year

Study	Reference
EE99	Foulon S, Brennan B, Gaspar N, et al. Can postoperative radiotherapy be omitted in localised standard-risk Ewing sarcoma? An observational study of the Euro-E.W.I.N.G group. Eur J Cancer. 2016 10;61:128-136
	Frank JA, Ranft A, Paulussen M, Juergens H, Kruseova J, Bauer S, Niggli F, Reichardt P, Dirksen U. Results for patients with sarcoma not otherwise specified and other diagnoses than Ewing sarcoma treated according to the Euro-EWING 99 trial. Pediatr Blood Cancer. 2017 Apr 24.
EpSSG NRSTS 2005	Bernadette Brennan, Gian Luca De Salvo, Daniel Orbach et al. Outcome of extracranial malignant rhabdoid tumours in children registered in the European paediatric Soft tissue Sarcoma study Group Non- Rhabdomyosarcoma Soft Tissue Sarcoma 2005 study – EpSSG NRSTS 2005 Eur J Cancer.2016;60:69-82
	Orbach D, Brennan B, De Paoli A et al Conservative strategy in infantile fibrosarcoma is possible: The European paediatric Soft tissue sarcoma Study Group experience. Eur J Cancer. 2016:57;1-9.
	Andrea Ferrari, M, Yueh-Yun Chi, Gian Luca de Salvo, Daniel Orbach, Bernadette Brennan et al. 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 and the Children's Oncology Group. Eur J cancer 2017 (in press)
EURAMOS-1	Marina N, Smeland Bielack S, Bernstein M, Jovic G, Krailo M, Hook J, Arndt C, van den Berg H, Brennan B, Brichard B, Brown K, Butterfass-Bahloul T, Calaminus G, Daldrup-Link H, Eriksson M, Gebhardt M, Gelderblom H, Gerss J, Goorin A, Goldsby R, Gorlick R, Grier H, Hale J, Sundby Hall K, Hardes J, Hawkins D, Helmke K, Hogendoorn P, Isakoff M, Janeway J, Jürgens H, Kager L, Kühne T, Lau C, Leavey P, Lessnick S, Mascarenhas L, Meyers P, Mottl H, Nathrath M, Papai S, Randall L, Reichardt P, Renard M, Safwat A, Schwartz, C, Stevens M, Strauss S, Teot L,Werner M, Sydes M, Whelan JS. Randomised Comparison of MAPIE vs MAP in patients with a Poor Response to pre-operative chemotherapy for newly-diagnosed high-grade osteosarcoma: results from the EURAMOS-1 trial. Lancet Oncol 2016
EUROEWING-99	Foulon S, Brennan B, Gaspar N, Dirksen U, Jeys L, Cassoni A, Claude L, Seddon B, Marec-Berard P, Whelan J, Paulussen M, Streitbuerger A, Oberlin O, Juergens H, Grimer R, Le Deley M-C. Can postoperative radiotherapy be omitted in localised

	standard-risk Ewing sarcoma? An observational study of the Euro-E.W.I.N.G group. Eur J Cancer. 2016;61:128-36. Epub 2016/05/14
ISKS study	Ballinger ML, Goode DL, Ray-Coquard I, James PA, Mitchell G, Niedermayr E, Puri A, Schiffman JD, Dite GS, Cipponi A, Maki RG, Brohl AS, Myklebost O, Stratford EW, Lorenz S, Ahn SM, Ahn JH, Kim JE, Shanley S, Beshay V, Randall RL, Judson I, Seddon B, Campbell IG, Young MA, Sarin R, Blay JY, O'Donoghue SI, Thomas DM; International Sarcoma Kindred Study.Monogenic and polygenic determinants of sarcoma risk: an international genetic study. Lancet Oncol. 2016 Sep;17(9):1261-71. doi: 10.1016/S1470-2045(16)30147-4
MMT95	D Orbach, V Mosseri, S Gallego, A Kelsey, C Devalck, B Brennan et al. Nonparameningeal head and neck rhabdomyosarcoma in children and adolescents: Lessons from the consecutive International Society of Pediatric Oncology Malignant Mesenchymal Tumor studies HeadNeck. 2017; 39 (1):24-31

Appendix 5

Major international presentations in the reporting year

Study	Conference details
EE2012	CTOS meeting November 2016:INITIAL REPORTS OF EURO EWING 2012 AND REECUR - INTERNATIONAL RANDOMISED CONTROLLED TRIALS OF CHEMOTHERAPY FOR NEWLY DIAGNOSED AND RECURRENT/REFRACTORY EWING SARCOMAS (ES) Bernadette Brennan, Martin McCabe ; Veronica Moroz et al - CTOS meeting November 2016
	TIMELINES ASSOCIATED WITH OPENING TWO CLINICAL TRIALS (EURO EWING 2012 AND REECUR) FOR EWING SARCOMA (ES) PATIENTS ACROSS EUROPE Bernadette Brennan, Martin Mccabe, Jennifer Anderton et al - CTOS meeting November 2016
EpSSG 2005 trials	ACCESS TO CLINICAL TRIALS FOR ADOLESCENTS WITH SOFT TISSUE SARCOMAS: THE ENROLMENT INTO THE EUROPEAN PAEDIATRIC SOFT TISSUE SARCOMA STUDY GROUP (EPSSG) PROTOCOLS A. Ferrari, A. Trama, A. De Paoli , C. Bergeron , J.H.M. Merks , M. Jenney et al - SIOP 2016 meeting
	LOCALIZED EPITHELIOID SARCOMA IN CHILDREN : AN EUROPEAN PAEDIATRIC SOFT TISSUE SARCOMA (EPSSG) STUDY N. Francotte , D. Orbach , I. Zanetti , B. Brennan et al - SIOP 2016 meeting
	DESMOID TUMORS IN CHILDREN AND ADOLESCENTS: THE EXPERIENCE OF THE EUROPEAN PAEDIATRIC SOFT TISSUE SARCOMA GROUP (EPSSG) D. Orbach , J. Daragjati , M. Van Noesel , B. Brennan et al - SIOP 2016 meeting
	Topotecan, vincristine and doxorubicin (TVD) for relapsed and refractory rhabdomyosarcoma; the UK experience. Adams M, Jenney M, McHugh K, Zanetti I, DeSalvo GL, Chisholm J - SIOP 2016 meeting
	Chisholm JC, Merks JH, Casanova M, Bisogno G, Orbach D, Gentet J, Thomassin Defachelles, A, Chastagner PB, Lowis S, Ronghe M, McHugh K, van Rijn RR, Hilton M, Bachir J, Furst-Recktenwald S, Geoerger B, Oberlin O. BERNIE: Open-label randomised phase II study of bevacizumab plus chemotherapy in pediatric metastatic rhabdomyosarcoma (RMS) and non-rhabdomyosarcoma soft tissue sarcoma (NRSTS). J Clin Oncol 34, 2016 (suppl; abstr 11054) - ASCO 2016
GEDDIS	Beatrice Seddon, Jeremy Whelan, Michael Leahy, Penella Woll, Fiona Cowie, Christian Rothermundt, Zoe Wood, Sharon Forsyth, Paul Patterson, Stephen Nash, Sandy Beare. GeDDiS: A prospective randomised controlled phase III trial of gemcitabine and docetaxel compared with doxorubicin as

	first-line treatment in previously untreated advanced unresectable or metastatic soft tissue sarcomas (EudraCT 2009-014907-29). Connective Tissue Oncology Society Annual Meeting, Salt Lake City, USA, November 2016.
VORTEX	Laura Forker, Piers Gaunt, Stefano Sioletic, Patrick Shenjere, Joely Irlam, Helen Valentine, David Hughes, Ana Hughes, Lucinda Billingham, Martin Robinson ,Catharine West. Evaluation of biomarkers in the UK phase III VorteX trial confirms importance of tumour hypoxia in soft tissue sarcoma, NCRI conference, 2016
EE99	Local Control and Survival in Ewing Sarcoma Patients: A Analysis of the Data of the Euro-EWING99 Trial Dimosthenis Andreou, Andreas Ranft, Georg Gosheger, Jendrik Hardes, Andreas Leithner, Arne Streitbuerger, Per-Ulf Tunn, Eva Wardelmann, Heribert Juergens, Uta Dirksen, International Society of Limb Salvage (ISOLS), Japan, 2017