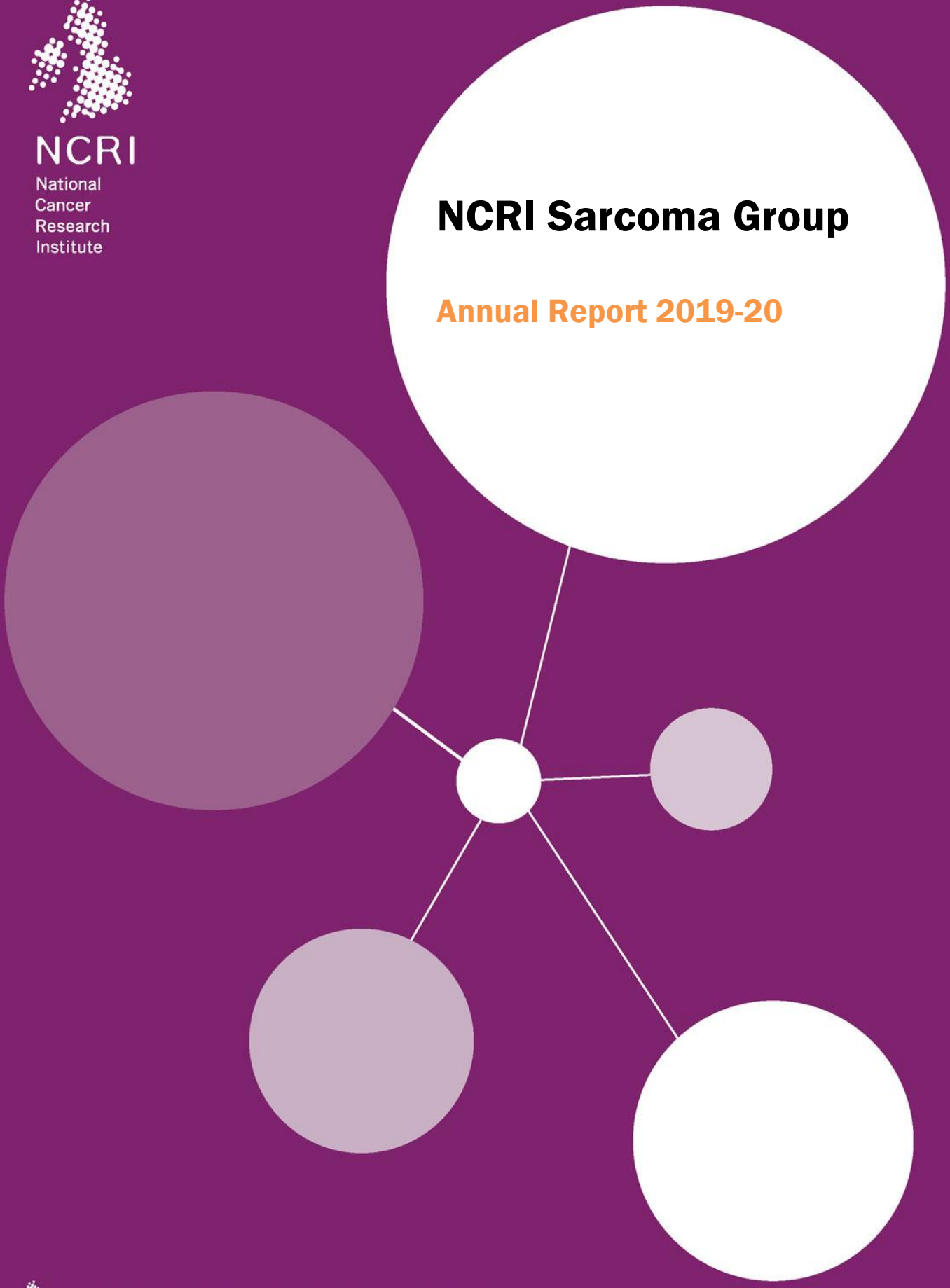
NCRI
National
Cancer
Research
Institute

NCRI Sarcoma Group

Annual Report 2019-20



Partners in cancer research

The NCRI Group Annual Reports 2019/2020 span the time period April 2019 – March 2020. The reports were submitted during a challenging time for all in the healthcare sector due to the COVID-19 pandemic. This has had an unprecedented impact on the activity of both the Research Group itself and wider research activities, ranging from the time available for research work versus clinical commitments to the funding of new trials and the recruitment of existing trials. Due to this the NCRI significantly extended the deadline for submission of annual reports and allowed the Groups to submit reduced reports, if time permitted, with the following sections at a minimum:

- Achievements (section 1 of the report)
- Funding Submissions over the last 12 months (section 5)
- Priorities and Challenges (section 7)

In addition to this, Consumer representatives of each Group were asked to only complete their sections if they feel able to. Most of our Consumers have submitted reports, however where reports have *not* been submitted this was due to extended periods of ill health, or additional work/home life constraints, as a result of COVID-19.

NCRI Sarcoma Group
Annual Report 2019-20

1. Top 3 achievements in the reporting year

Achievement 1

Following closure of EE2012 earlier in 2019, the first results of the trial were presented at Connective Tissue Oncology Society (CTOS) 2019, and further results have been accepted for an oral presentation at American Society of Clinical Oncology (ASCO) 2020. These results, for the first time in Ewing sarcoma (ES), established a standard of care for all ES internationally as the "experimental" arm had superior progression free survival (PFS) and overall survival (OS) and indeed less toxicity. This will serve as the backbone chemotherapy arm to which we hope to add a targeted agent in the next European Ewing sarcoma trial EE20XX the National Cancer Research Institute (NCRI) group is developing

Achievement 2

rEECur is the first and largest randomised control trial in refractory / relapsed ES, with a novel MAMS design, and originally 4 chemotherapy arms. The first arm GD was dropped and presented in ASCO 2019, the second arm IT was dropped in Feb 2020, and is to be presented ASCO 2020. The data linking overall response (OR) and PFS in rEECur will be presented at ASCO 2020, demonstrating that OR is not a predictor PFS.

Achievement 3

Another flagship trial of the Group is RMS 2005, which published its results of the second randomisation in The Lancet Oncology in 2019, demonstrating the benefit of maintenance chemotherapy for high risk rhabdomyosarcoma, now adopted as standard of care throughout Europe and USA. The successor study FaR-RMS, another Group development, is ready to open in many UK centres, and has secured a further targeted agent, Regorafanib, for the Phase II relapsed rhabdomyosarcoma component of this large international umbrella trial.

2. Structure of the Group

Having rotated off the Group after the last report, Professor Bernadette Brennan was appointed the Chair of the Group in February this year. The Young Onset Soft Tissue Sarcoma (YOSS) Subgroup also has a new Chair, Dr Henry Mandeville, who was also welcomed to the main Sarcoma Group, as was Dr Sandra Strauss as the new Chair of the Bone Tumour Subgroup. They both bring a wealth of sarcoma research experience, and importantly for our strategy, active trial development.

The membership of the Sarcoma Group continues to evolve every year. The feedback from the Quinquennial Review (QQR) Panel Report in 2018 highlighted the number of different specialities within the Group, in particular the Bone Tumour Subgroup, which was described as a great asset to the Group. The main Sarcoma Group now consists of 5 clinical oncologists, 4 surgeons (including a retroperitoneal sarcoma surgeon), 4 medical oncologists, 3 paediatric oncologists, 2 consumer representatives, 2 pathologists, 2 scientists, 2 trainee representatives (clinical research fellow and trainee orthopaedic surgeon), a medical physicist, a statistician and a clinical nurse specialist from a wide geographical distribution throughout the UK. The diversity of membership is also represented within the YOSS, Bone, and Soft Tissue Sarcoma (STS) Subgroups.

3. Sarcoma Group & Subgroup strategies

Sarcoma Group

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

For STS in the last year several new studies have opened, though many are sponsored by pharma but do allow access to new targeted drugs or therapies. They cover the specific sarcomas – synovial sarcoma - 2 – specific targeted therapies with adaptive T cells for patients in 2nd line with no realistic chance of cure. Gastrointestinal Stromal Tumour (GIST) also benefits from the pharma partnerships with a phase II study after failure of first line therapy. While sarcomas are rare an orphan tumour among these – Desmoids has had very little in the way of therapeutic trials. Again, a novel therapy Nirogacestat is being assessed as first line therapy.

The International Rare Cancers Initiative (IRCI) is a strategic collaboration between Cancer Research UK (CRUK) and UK National Institute for Health Research Cancer who developed HGUtS in uterine sarcomas – centres have also opened in Europe and USA and is sponsored by the EORTC. This trial allows an extremely rare sarcoma entry into a randomised study with a targeted agent cabazantinib, while recruitment has been difficult it remains open. ANNOUNCE recruited very successfully in UK and internationally but despite the promise of Olaratumab from the phase II data the results in the end didn't show a benefit for olaratumab. One of our flag ship trials FAR-RMS should be open but issues around the database outside the CTU prevented this compounded by COVID 19. However, many of the UK centres are ready to open once the CTU gives the green light as they have all the necessary local approvals.

For all sarcomas assessing the benefits of therapy also requires good QoL tools and hence a new academic study from the Royal Marsden team has opened. The development of a paediatric version of the Sarcoma Assessment Measure (SAM-Paeds): a specific tool for assessing quality of life in children with sarcoma' is being led by Dr Madeleine Adams and Professor Meriel Jenney from the Children's Hospital for Wales and Dr Rachel Taylor from University College London.

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

The following trials are currently under development:
EE20XX – successor trial in Ewing sarcoma(ES) to EE2012 (interventional and non-interventional arms).The EE20XX trial is a comprehensive study in newly diagnosed Ewing sarcomas with multiple randomised questions at multiple stages in a phase III study with three principal aims. These are to evaluate:

- the introduction of multiple tyrosine kinase inhibitors (TKI) into current standard regimens in newly diagnosed metastatic Ewing sarcoma- hopefully secured lenvatinib
- the dose escalation of radiotherapy to localised poor risk disease to improve overall survival by reducing both local and systemic events
- the addition of maintenance treatment after the end of consolidation therapy to reduce events and improve overall survival
- informative biomarkers of disease status and response at diagnosis and throughout the disease course, are predictive of minimal residual disease and hence predictive of disease recurrence
- whether DW-MRI and FDG PET- CT response assessment following induction chemotherapy is a prognostic biomarker for local failure and/ or survival, and the accuracy (specificity/sensitivity) of DWIBS in the staging of Ewing sarcoma patients

EpSSG MYCKIDs study - Molecular identity card for kids, adolescent and young adults with non-rhabdomyosarcomas soft tissue sarcoma (non- interventional)

- This study aims to coordinate and collect clinical, pathological and biological data on pediatric and AYA affected by these very rare entities in Europe, within the framework of the European paediatric Soft tissue sarcoma Study Group (EpSSG). The main objectives are to examine the role of biology in predicting outcome (histologic grading, CINSARC, genomic index) [group A] and better characterize undifferentiated entities [groups A and B]. Additional aims are to provide an integrated central pathology review with molecular profiling, for the diagnosis of all NRSTS in Europe.- submitted to Fight Kids Cancer grant call 4-2020

DESMOVER (EpSSG) (interventional)

- Multicenter prospective randomized Phase II trial evaluating the efficacy and safety of oral methotrexate-vinorelbine *versus* methotrexate-vinblastine in children and young adults with progressive desmoid tumor. Protocol writing stage.

Increase studies in bone sarcoma

The research group has studies opened or developing studies in the 4 main bone tumours:

1. Osteosarcoma – ICONIC opened to recruitment in October 2019 and is recruiting well.
2. Ewing sarcoma - EE2012, closed earlier than planned due to positive results in May 2019. The first results of the trial were presented at CTOS 2019, and further results have been accepted for an oral presentation at ASCO 2020. Developing the successor study EE20XX.
   rEECur, the first and largest randomised control trial in refractory/relapsed ES, with a novel MAMS design, and originally 4 chemotherapy arms. The first arm GD was dropped and presented in ASCO 2019, the second arm IT dropped Feb 2020, and to be presented ASCO 2020. The data linking OR and PFS in rEECur will be presented at ASCO 2020, demonstrating that OR is not a predictor PFS.
3. Chondrosarcoma – ctDNA and cartilage tumours has been a phenomenal success and has competed recruitment ahead of schedule. Further studies are now in development
4. Two studies are open for chordoma. Guiding Chordoma Treatment through Molecular Profiling: A National Cohort Study has nearly finished recruitment.
   A Phase 2, Single Arm, European Multi-centre Trial Evaluating the Efficacy of Afatinib as First-line or Later-line Treatment in Advanced Chordoma opened in 2019 and is recruiting well.

Further develop the Sarcoma Group portfolio

While partnership with pharma has allowed the development of studies as described above in soft tissue sarcoma such as in synovial sarcoma and desmoids, there remains a significant gap for STS in particular the lack of phase III randomised studies introducing new therapies either nationally or indeed internationally. This will be the priority going forward and the main focus of our strategy meeting in 2020.

There is clearly studies in the wider NCRI portfolio that we contribute to such as SM paeds and the about to open ESMART, but more work on the portfolio needs to be done firstly to improve its accuracy, add other studies and indeed question its validity if not useful.

Raise awareness and profile

The Group continues to present abstracts at international and national meetings for studies developed within the research group- ASCO, CTOS, SIOP and BSG. The Group 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 research group to engage with the sarcoma community to uncover areas of unmet research need.

Develop trials in key research priority areas

1. Surgery – There is a lack of specific surgical questions that could be answered by a randomised question makes securing funding difficult for a stand-alone study. The focus on surgery should perhaps change to a focus on local control and for sarcomas the interaction between surgery and radiotherapy; hence the questions with regard to this developed in FaR-RMS and in the next ES study EE20XX. The Group has added surgical and radiological questions regarding surgical margins, function of reconstruction and radiological assessment of response in the ICONIC study for Osteosarcoma and views this as a viable alternative strategy to stand alone surgical studies. The STS Working Party is interested in incorporating a randomised question on identifying biomarkers of poor wound healing and randomising interventions prior to surgery, especially as pre-operative radiotherapy has a wound healing problem in over 30% of cases but this is yet to come to fruition.
2. Osteosarcoma/Chondrosarcoma – The Group has developed studies for both of these tumour types, which have been funded and are open. Follow up studies are currently being discussed.
3. QOL/Follow up – The SAMs trial is focused on PROMS for sarcoma patients. This aims to recruit 1000 patients and continues to recruit well. Stratification Of Sarcoma Pathways; improving diagnostic and follow up pathways for patients with extremity sarcoma study is currently under development., as well as the SAM-Paeds trial is in development Translational
4. The Group has excelled in increasing translational research in either standalone studies or embedded to larger studies. Translational studies are available in Osteosarcoma, Chondrosarcoma, Ewings, Chordoma and STS. The group continues to engage with GECiP and SPECTA.

Strengthen UK wide and international working

Given the size of the national and international community of sarcoma research the Group 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 Group 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 research group.

The Group also regularly interacts with other NCRI Groups with members sitting on Consumer Forum, SPED Advisory Group, Children's Group and Teenage & Young Adult (TYA) & Germ Cell Tumours (GCT) Group 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 Group has benefitted from interaction with Children's Group, Gynaecological

Group, Living With & Beyond Cancer (LWBC) Group and TYA & GCT Group either in the main meetings or via interaction with subgroups.

Sarcoma Group structure and function

The strength of the Group 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 Bone Cancer Research Trust (BCRT), attend the meetings, which provides valuable feedback to the members and helps the charities consider areas of unmet research needs. The Group 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 main group or subgroups.

Patient and Public Involvement and Impact

PPI has a strong impact/involvement in the trials developed or in development through the EEC, EpSSG and the ICONIC study. This is also supported by the sarcoma charities involvement in these groups and the Group – BCRT and Sarcoma UK.
See also consumer report.

Adult Soft Tissue Sarcoma Subgroup (Chair, Aisha Miah)

Strategic objective 1

Research mapping for systemic therapy, radiotherapy and surgery to determine current trial activity in the UK.

Strategic objective 2

Translational workshop undertaken to improve collaborative network across UK.

Strategic objective 3

Develop studies in soft tissue sarcoma through national collaboration with involvement with charitable partners and industry partners where possible.

Focus areas embedding parallel biological studies and incorporating analysis from the whole genome sequencing proposed for soft tissue sarcomas:

1. Early diagnosis

2. Treatment of local disease
3. Treatment of metastatic disease

Bone Tumour Subgroup (Chair, Dr Sandra Strauss)

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

The ICONIC study, developed through the Subgroup, was opened to recruitment on 26 October 2019. To date, 24 patients have been recruited. Ideas for further sub-studies were discussed at the investigator's meeting held in Glasgow aligned to the BSG in February 2020. It was clear further funding would be required to progress these and that the focus for the next year would be on recruitment to determined feasibility of this as a long-term strategy.

A closed meeting with AstraZeneca was set up to be held alongside the next Bone Subgroup meeting to increase opportunities for collaboration with industry partners as has been identified as a challenge for sarcomas. This has been cancelled due to COVID-19 but we hope to reschedule towards the end of 2020.

Develop studies where there were none, for osteosarcoma and chondrosarcoma

Both these have been successfully realised. The current chondrosarcoma study is nearing completion. A workshop was held in November 2019 to develop ideas for future studies. This set priorities for development of biomarker and interventional studies, funding will also need to be identified. An update is expected at the next Bone Subgroup meeting scheduled for June 2020 (we are aiming for a shortened web-linked meeting).

Promote national collaboration in the development and delivery of studies

National collaboration continues to be a key strategic aim and is evidenced by the attendance at meetings and the development and funding of multicentre research. In addition, the Bone Subgroup membership has been updated with new members representing the wider multi-disciplinary team. These include: Dr Suzanne Gatz a translational paediatric oncologist from Birmingham Children's Hospital, Ms Harriet Brandford-White, a new trainee (and surgical) representative, Mr Mike Parry, surgeon from the Royal Orthopedic Hospital in Birmingham and Dr Martin McCabe a paediatric oncologist from the Christie Hospital, who is also on the TYA & GCT Group.

The following have rotated off and were thanked for their contribution: Professor Bruce Morland, Dr Matthew Sydes, Professor Keith Wheatley and Professor Jeremy Whelan (who will remain an affiliate member).

Develop the next European Ewing Study EE 20XX

The first results of EE2012 were presented at the Connective Tissue Oncology Society meeting in Tokyo in November, defining a new standard of care for patients with newly diagnosed ES. Also to be presented at ASCO in 2020.

This has allowed significant progress in the development of EE20XX with regular meetings supported by the European Ewing's Consortium (EEC). Funding for the Consortium ended in September 2019, but the activities are currently being supported by short term funding for a project manager. Dr Strauss has been appointed chair of the EEC executive committee, with a remit to support development of international Ewing sarcoma clinical trials. A protocol draft is now nearing completion to apply for funding within the next 6-12 months depending on funding calls and availability.

A CRUK application to extend the rEECur study has been successful, with an abstract presented at ASCO in 2019, dropping the first arm of the study and further results to be presented at ASCO in 2020.

Young Onset Soft tissue Subgroup (YOSS) (Chair, Dr Henry Mandeville)

Open a first line study in Rhabdomyosarcoma across all ages in UK centres and European centres 2. Build in current relapse studies in RMS using VIT as the new standard of care

FaR-RMS: An overarching study for children and adults with localised and metastatic Frontline and Relapsed Rhabdomyosarcoma. This study is about to be opened in the UK, Europe and Australasia; delayed due to the COVID-19 crisis.

The three principal aims of the study are to evaluate:

- systemic therapy through the introduction of new agent combinations regimens in the most advanced disease states: Very High Risk (VHR), High Risk (HR) and Relapse
- the duration of maintenance therapy
- radiotherapy to improve local control in VHR, HR and Standard Risk (SR) patients and to treat metastatic disease

In addition the study will evaluate:

- risk stratification through the use of PAX-FOXO1 fusion gene status instead of histological subtyping
- the use of FDG PET-CT response

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

EpSSG MYCKIDs study: Molecular identity card for kids, adolescent and young adults with non-rhabdomyosarcomas soft tissue sarcoma (non- interventional). This study aims to coordinate and collect clinical, pathological and biological data on paediatric and AYA (age < 30 years) affected by these very rare entities in Europe, within the framework of the European paediatric Soft tissue sarcoma Study Group (EpSSG). The main objectives are to examine the role of biology in predicting outcome (histologic grading, CINSARC, genomic index) [group A] and better characterize undifferentiated entities [groups A and B]. Additional aims are to provide an integrated central pathology review with molecular profiling, for the diagnosis of all NRSTS in Europe - submitted to Fight Kids Cancer grant call 4-2020

Build on the outcomes of other rare sarcomas from the NRSTS 2005 study to develop further clinical trials, specifically Rhabdoid tumours at all sites, and Desmoids

DESMOVER (EpSSG) (interventional)

- Multicenter prospective randomized Phase II trial evaluating the efficacy and safety of oral methotrexate-vinorelbine versus methotrexate-vinblastine in children and young adults with progressive desmoid tumour. Protocol writing stage.

A multi-centre, open-label, randomized, phase Ib/II dose-finding study of EZH2 inhibitor Tazemetostat in paediatric, teenagers and young adult subjects with malignant rhabdoid tumours at any site at diagnosis in combination with backbone chemotherapy (vincristine, doxorubicin, cyclophosphamide – VDC – and ifosfamide, etoposide – IE).

- Study Centres- 20 ITCC and Phase I accredited Paediatric /TYA centres
- Approaching Epizyme (pharma) with proposal and ITCC have discussed the proposal.

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

This will be achieved in FaR-RMS as above and MYCKIDs - a successor to EpSSG NRSTS 2005 (as above).

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, wherever possible.

4. Task groups/Working parties

There were no task groups or working parties within the reporting year.

5. Funding applications in last year

Table 2 Funding submissions in the reporting year

Study	Committee & application type	CI	Outcome	Level of Group input	Funding amount
Cancer Research UK					
May 2019					
rEECur: International Randomised Controlled Trial of Chemotherapy for the Treatment of Recurrent and Primary Refractory Ewing Sarcoma	Clinical Trial Award (full)	Dr Martin McCabe	Conditionally supported		
November 2019					
None					
Other committees					
Study	**Committee & application type**	**CI**	**Outcome**	**Level of Group input**	**Funding amount**
Development of a paediatric version of the Sarcoma Assessment Measure (SAM-Paeds): a specific tool for assessing quality of life of children with sarcoma	CCLG- research proposal grant (also successful with Sarcoma UK)	Maddi Adams , Meriel Jenny	Supported	Devised study and will be PIs	£80 k

6. Consumer involvement

Phillip Green

Phil is one of two Consumer Members of the NCRI Sarcoma Group and has been in post since August 2018. In addition to his main group membership, Phil is now a consumer representative on the Bone Tumour Subgroup, having recently accepted an invitation to participate from its new Chair. Phil is the Consumer Member of the Trial Management Group for the ICONIC Study led by Dr Sandra Strauss and funded by the Bone Cancer Research Trust. He has critiqued and edited the patient information drafts, resulting in an improved publication that is now perceived to be optimal to ensuring patient understanding of the study concepts, with the aim that patient recruitment will be maximised. Phil has also completed a similar exercise by commentating on and modifying the trial documentation intended to be sent to patient's GPs; the purpose being to collate information relating to the pre-diagnostic patient journey. GP supplied data will be key to the success of one component of the study. This study is now open and recruiting well and Phil attends and contributes to regular TMG meetings as the patient advocate.

Phil has become an active member of Sarcoma PAtient EuroNet (SPAEN); a well established pan-European sarcoma patient advocacy group. Having attended the annual conferences in Athens in 2019 and Milan in 2020 generating a number of excellent European patient and professional contacts, he has been subsequently been selected to participate in a European-wide project, that aims to develop a strategy to improve outcomes for sarcoma patients. In a collaborative effort of patient advocates, patients, carers and sarcoma experts (represented by the EORTC Soft Tissue and Bone Sarcoma Group) the intention was to create a Sarcoma Research White Paper, or similar publication, highlighting the top 10-20 consumer-determined research priorities in sarcoma. This study is now complete and was due for publication by Olga Husain (EORTC) following its presentation in February, at the 2020 SPAEN conference in February.

There was some disconcertion regarding the lack of inclusion of presentations relating to primary bone cancers (PBCs) at the 2020 SPAEN conference, resulting in two positive outcomes. The first was for Phil to accept an invitation to advise on PBCs at SPAEN's forthcoming 5-year strategy meeting with the main board members. The second was to co-lead the formation of a pan-European SPAEN Bone subgroup, Bone Sarcoma Patient Org (also including representation from the USA, Chile, India and South Africa). The group strategy is to initially encourage sarcoma conference organisers to embed a significant bone component within their programmes. To date we have received positive responses in this regard from both Professor Paulo Casali, board member and conference organiser for ESMO and Marcus Wartenberg, board member and chair of SPAEN. A similar approach has been made to the organisers of the ESMOS conference. This organisation also has membership representation from the Bone Cancer Research Trust and there is an intention to work collaboratively to improve early diagnosis of PBCs.

As a patient advocate and GP Ambassador for the Bone Cancer Research Trust, Phil is making a significant contribution to their GP Awareness programme. To date, this has involved attendance at several 'brain-storming' meetings to develop the trusts strategy and thus establish a number of tangible outcomes, some of which have already been implemented. These include a collaborative programme involving students from Sheffield University Medical School, who have not only embarked on a voluntary sarcoma lab placement programme but who have also

contributed to the development of Red Flag Symptom flashcards for GPs, critiqued by Phil before publication. Additional work on the BCRT GP Awareness programme is ongoing and interim report will expand on the detail as it begins to demonstrate impact.

Phil attended the WeCan Conference in Frankfurt in July 2019 and is producing a report detailing the significant generic learning points from this with the NCRI Consumer Group. He was also a consumer representative at the NCRI Conference in Glasgow in November 2019. There was, as ever, a notable lack of presentations/posters relating to sarcoma research, which Phil feels should be a consideration for the NCRI Sarcoma Group to address going forward.
A further addition to Phil's educational development is that I have been selected by SPAEN, to be their representative on the WECAN Evidence-Based Advocacy: Evidence generation and publication project. The course content is outlined: The training programme consist of a 9-months blended learning programme of webinars and a 2-day in person workshop in January 2021, with the webinars recorded and made available on the WECAN website. This will be followed by 2-months of tailored individual coaching on one evidence generation project that each WECAN member may take on at the end of the programme, in order to develop a concrete evidence-generation project for their organisation to take forward in an area of strategic importance.

In collaboration with Envision, WECAN is also developing a specific training module on patient involvement in publications, which will be taught in the training programme but will also be made available open access on the WECAN website. WECAN will also include the existing knowledge in evidence generation from a number of patient organisations to share best practice across the cancer community. WECAN will build capacity, knowledge, and resources so that each WECAN member organisation can generate and publish their own data.

Content development has started in January 2020, with WECAN member trainees nominated in April 2020. The training programme will start in early May 2020 and run until March 2021. Each WECAN member organisation can nominate one person who will be trained and coached to increase the capacity for evidence generation in their network. This person will then act as expert in evidence-based advocacy within their community.

Phil's strategy with this project is to:

- Utilise the expertise to work with the BCRT to measure the impact of its GP awareness campaign
- Continue to look at the aforementioned impact when the campaign is adopted by our European partners and
- Act as lead patient advocate mentor for SPAEN with regard to research into the overall impact of patient advocacy (there is currently no hard evidence to suggest that it is beneficial in the context of research trials).

Phil has established regular contact with his scientific mentor via NCRI Group Meetings, Trial Management Group Meetings and via telephone. She has informally but positively commentated on his contributions to Group activities to date and these have been formally recognised by the Group as a whole, during its meetings.

Terence Weldon

No consumer report submitted – please refer to page 2.

7. Priorities and challenges for the forthcoming year

Priority 1 To develop an all age study for all patients with STS in UK – clinical/biological /QoI – which acts a platform to develop therapeutic interventions and generate hypothesis for future studies and improves patient's outcomes.
Priority 2 To develop and acquire funding for the successor trial to EE2012 in ES for all ages.
Priority 3 To look at building an Osteosarcoma collaborative group within Europe and USA to develop future therapeutic interventions in OS perhaps generated from the current ICONIC study.
Challenge 1 Availability of new drugs even for academic studies to test in sarcoma patients.
Challenge 2 In view of the COVID 19 pandemic and the reliance of the sarcoma community on UK sarcoma charities for funding research – the reduction in available funds for any future planned research.
Challenge 3 Recruitment of all ages into available sarcoma trials in particular the TYA population.

8. Collaborative partnership studies with industry

Bone Tumour Subgroup

A closed meeting with AstraZeneca was set up to be held alongside the next Bone Tumour Subgroup meeting to increase opportunities for collaboration with industry partners as has been identified as a challenge for sarcomas. This has been cancelled due to COVID-19 but we hope to reschedule towards the end of 2020.

EE20XX, for the next ES study interactions and protocol development with pharma has occurred to gain access to a tyrosine kinase inhibitor for phase Ib part of the study and if successful into a phase III study.

YOSS Subgroup

FaR-RMS – discussions with Bayer has secured the targeted agent, Regorafanib, for the Phase II relapsed rhabdomyosarcoma component of this large international umbrella trial.

9. Appendices

Appendix 1 - Sarcoma Group and Subgroup strategies

A - Sarcoma Group Strategy
B - Adult Soft Tissue Sarcoma Subgroup
C - Bone Tumour Subgroup Strategy
D - Young Onset Soft-tissue Sarcoma Subgroup Strategy

Appendix 2 - Top 5 publications in the reporting year

Professor Bernadette Brennan (Sarcoma Group Chair)

Appendix 1

Sarcoma Group and Subgroup Strategies

A – Sarcoma Group 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 - Adult Soft Tissue Sarcoma Subgroup

No Strategy

C – 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.

D – Young Onset Soft-tissue Sarcoma Subgroup Strategy

The Subgroup 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, Europe and other countries who are part of the EpSSG

2. To build on current relapse studies in RMS using VIT as the new standard of care- 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 in summer 2020 following Covid 19 related delays..

2. See above

3. To develop MYKIDS and DESMOVER

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

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

6. To open the prospective MYCKIDs: Molecular Identity Card for kids, adolescent and young adults with non-rhabdomyosarcoma soft tissue sarcoma cohort study which incorporates biological questions relevant for all the NRSTS subtypes

7. To increase the TYA population in sarcoma studies- this will be achieved by extending the upper age range for study entry; FaR- RMS includes adults with no upper age limit, and MYCKIDs includes young adults up to 29 years old.

Appendix 2

Top 5 publications in the reporting year

Trial name & publication reference	Impact of the trial	Group involvement in the trial
1. Vinorelbine and continuous low-dose cyclophosphamide as maintenance chemotherapy in patients with high-risk rhabdomyosarcoma (RMS 2005): a multicentre, open-label, randomised, phase 3 trial. Bisogno G, De Salvo GL, Bergeron C, Gallego Melcón S, Merks JH, Kelsey A, Martelli H, Minard-Colin V, Orbach D, Glosli H, Chisholm J, Casanova M, Zanetti I, Devalck C, Ben-Arush M, Mudry P, Ferman S, Jenney M, Ferrari A; European paediatric Soft tissue sarcoma Study Group.Lancet Oncol. 2019 Nov;20(11):1566-1575	Vinorelbine and continuous low-dose cyclophosphamide is now standard of care in Europe and USA for patients with RMS	Designed and acquired funding for the trial and multiple members were CI/PI and recruited patients.
2. Cediranib in patients with alveolar soft-part sarcoma (CASPS): a double-blind, placebo-controlled, randomised, phase 2 trial. Judson I, Morden JP, Kilburn L, et al. Lancet Oncol. 2019;20(7):1023-1034.	Given the high incidence of metastatic disease and poor long-term prognosis of ASPS, together with the lack of efficacy of conventional chemotherapy, our finding of significant clinical activity with cediranib in this disease is an important step towards the goal of long-term	Designed and acquired funding for the trial and multiple members were CI/PI and recruited patients

	disease control for these young patients. Future clinical trials in ASPS are also likely to involve immune checkpoint inhibitors, and should not include conventional chemotherapy	
3. Inflammatory myofibroblastic tumor: The experience of the European pediatric Soft Tissue Sarcoma Study Group (EpSSG). Casanova M, Brennan B, Alaggio R, Kelsey A, et. al. Eur J Cancer. 2020 Mar;127:123-129	This study demonstrated a good overall prognosis for IMT, even for initially unresectable disease and in ALK-negative cases. Chemotherapy is still a valid option for advanced disease. Larger studies involving both pediatric and adult patients are needed to clarify the role of ALK inhibitors.	Designed and acquired funding for the trial and multiple members were CI/PI and recruited patients
4. Effect of Doxorubicin Plus Olaratumab vs Doxorubicin Plus Placebo on Survival in Patients With Advanced Soft Tissue Sarcomas: The ANNOUNCE Randomized Clinical Trial. Tap WD, Wagner AJ, Schöffski…. Jones RL; ANNOUNCE Investigators. JAMA. 2020 7;323(13):1266-1276	Demonstrated that large randomised trials need to be done to truly examine the role of targeted agents with conventional chemotherapy	Members were PIs and recruited patients from UK centres
5. The Challenge of Sarcomas - the Patient Advocacy Group Perspective Roger Wilson Clinical Sarcoma Research. DOI: 10.1186/s13569-019-0121-6 https://rdcu.be/bKM3k	Roger is a long term member and ambassador for Sarcoma and puts the case in an excellent manner for the role of patient advocates in sarcoma and indeed cancer research	Roger Wilson member of the research group