International Osteosarcoma Research Symposium

31 January 2019

Goodenough College, Mecklenburgh Square, London WC1N 2AB

In Memory of Frankie Biggs

Outputs and Actions from the Workshop

Executive Summary

The International Osteosarcoma Research Symposium was organised in memory of Frankie Biggs due to concern that outcomes for patients with osteosarcoma remain unacceptable. The aim of the day was to bring a range of experts together, both from the UK, Europe and the USA to understand progress to date and to prioritise and harmonise actions needed to bring about a step change in osteosarcoma patient outcomes.

The day highlighted several areas of focus; however, the overwhelming feeling was that there is currently a lack of collaboration and co-ordination across all areas and addressing this is fundamental to making progress.

It is imperative that a more collaborative approach is taken to research. Future research should be;

- Multidisciplinary – harnessing the expertise of many disciplines such as bone biology, medicinal chemistry, in-vivo techniques and clinical oncology.
- Collaborative; between individuals and groups, both nationally internationally
- Funded in a collaborative and co-ordinated manner by multiple charities and organisations to maximise outputs
- Focused on key areas of priority, identified by the symposium attendees, such as early diagnosis, travel and training fellowships, PhD studentships and Early Career fellowships.

The International Osteosarcoma Research Symposium was a huge success, the impact of this meeting is already being seen through increased research applications. The meeting has highlighted that there is a significant body of work to be done in order to see positive change and funding is needed to co-ordinate this programme of work. Funding of an annual symposium will be a key component of maintaining collaboration and ensuring that maximum impact from ongoing research is made and disseminated.

We are grateful to Mr Paul Britton for his generous sponsorship of this meeting.

Purpose

The International Osteosarcoma Research Symposium began with short presentations, aimed at fully understanding both the clinical and research landscape in osteosarcoma across the UK with an international perspective provided by experts from Germany and the US. These presentations were followed by a workshop, facilitated by Dr Ian Lewis, Head of Strategy and Initiatives, NCRI. The aim of this workshop was to bring delegates with different expertise together to discuss gaps and challenges in osteosarcoma treatment and research, the opportunities and actions needed to overcome these and to think about priorities for future funding and research. There was a huge amount of debate and many ideas and suggestions were put forward. This document firstly lists the main themes from these discussions, followed by a table to summarise all the topics/ideas recorded during the day.

Priorities for funding and actions form workshop.

The workshop generated much discussion, which highlighted 4 main areas of priority. These were mainly around the areas of enhancing collaboration and funding / training opportunities to accelerate osteosarcoma research and trials. These, and actions needed to address these have been listed below:

1. NETWORKING AND COLLABORATION

Improve collaboration and accelerate impact of OS research through:

- Funding an annual interdisciplinary networking meeting
- Ensuring presence at international meetings to enhance international collaboration.
- Linking to other national osteosarcoma research and clinical groups and European Bone Sarcoma Networking Group.
- Potentially funding an international meeting to enhance collaboration
- Development of a UK-hub as part of a website to map researchers and activities, models of osteosarcoma research and dissemination of results
- Funding calls aligned to ongoing initiatives / infrastructure such as ICONIC and GeCIP
- Development of partnerships between charities and exploring co-funding arrangements

2. CLINICAL RESEARCH

- Facilitate national and international collaboration to develop therapeutic studies in osteosarcoma, aligned with the NCRI Sarcoma Research Group and with PPI
- Fund meetings to bring together experts to develop protocols and potential programme grants
- Fund meetings and/or specific calls focusing on:
    - Local therapy
    - Delayed diagnosis
    - Patient experience
- Explore opportunities to enhance engagement with academic drug development departments and industry

3. TRAINING AND EDUCATION

Provide dedicated funding for:

- Early careers fellowships ~£500k
- PhD studentships in osteosarcoma - particularly pathology and bioinformatics
- Travel fellowships:
    - to allow opportunities to enhance skills by funding visits to other (national or international) laboratories, which could be used to bridge skill/techniques gaps.
    - to allow clinicians to attend international meetings and report back eg ASCO, ESMO, AACR
    - These could be called the ‘Frankie Biggs: travel fellowships / grants’.
    - Grant winners could present the feedback from these meetings at the annual meeting

Provide development opportunities by:

- Setting up a national junior researcher network
- Providing opportunities for trainees to join charity grant review panels

4. PRE-CLINCAL RESEARCH

- Funding calls specifically for the development of clinically relevant genetically characterised osteosarcoma models and ongoing infrastructure to support these.
- Have as a condition of funding that these models be provided as a resource for the community
- Sharing of techniques and resources through a hub/website

Full overview of topics and ideas raised during the workshop

The table below details all items identified during the workshop discussions. During the workshop, delegates split into a number of groups and worked together to identify the main barriers and gaps in the osteosarcoma research landscape and what can be done to address these in order to accelerate research and improve outcomes for osteosarcoma patients. The documents produced during these group discussions have been collated and entered in the table below. Points identified have been split in to common themes with Opportunities & Actions aligned to each Gaps & Barriers identified.

Barriers & Gaps	Opportunities & Actions
1. Staffing/Skills	
1. Segregation and Isolation a. Researchers have own areas of expertise and often narrow focus with little perspective of global picture b. Variation across the country regarding interests and expertise and engagement with the wider community c. London-centric **2. Skills gap** a. Lack of input from bone biologists b. Little of input from wider clinical community such as GPs and anaesthetists c. Limited engagement with allied health professionals such as physiotherapists and occupational therapists d. lack of pathologists and bioinformaticians	**1. Segregation and Isolation -** Interest amongst room for better linking/collaboration a. Enhance communication and collaborative opportunities across the community b. Provide a platform to map people, skills and opportunities to facilitate collaboration c. Enhance opportunities for sharing and dissemination of research to improve relationships across community **2. Skills gap** Opportunity to form collaborations with other groups a. The Bone Research Society is well established and so there is potential to invite bone biologists and work collaboratively to enhance inter-disciplinary research b. Expand GP involvement through the recruitment of a GP on the NCRI Sarcoma Research Group

e. Should we / can we involve patients – are there any gaps? **3. Others** a. Personalities - protective attitudes, lack of cohesion and collaboration, easy to focus on clinical research and not include basic researchers or those outside sarcoma centres b. Difficult for clinicians to get dedicated research time	c. There are engaged research physiotherapists working within sarcoma. These should be included in future meetings d. Active PPI community who are keen to engaged **3. Others** These issues are difficult to address but have been taken in to account → ACTIONS 1. Identify skills gap to accelerate osteosarcoma research 2. Invite individuals needed to future meetings 3. Have dedicated priming / small grants to visit different laboratories or clinical teams to learn skills/techniques 4. Create an osteosarcoma PPI group 5. Provide opportunities for networking and meeting with dedicated time to accelerate research 6. Provide a platform to map skills and interests
2. Funding	
1. Lack of it! 2. Little /no co-ordination between charities with regards to calls and priorities 3. Limited/no funding available for training and education 4. No funding available for awareness 5. Difficult to keep researchers interested in OS due to challenges in getting funding	1. Work with NHS and larger charities to leverage funding. a. Work collaboratively as a network to secure large programme grants 2. Charities to work closely with research & clinical community and also the NCRI Sarcoma Research Group to discuss funding calls/priorities a. Charities to meet to agree funding priorities

6. Some projects do not fit in to standard funding calls and it is hard to get these funded 7. Hard to get funding for 'unsexy' research such as RT and QOL	3-7. New types of grants could be developed to fund projects / training that currently sits outside standard calls → ACTIONS • Map of funding opportunities and types of grants available • Scope potential of developing new grants/funding calls to meet specific and priority needs
3. Trials	
1. Hampered by previous experience in EURAMOS - need new people to lead 2. Lack of new treatments and testable clinical questions 3. Need for international collaboration in trials makes them challenging 4. Time taken for phase 3 trials unacceptable 5. Translation gap - good research ideas hard to progress to clinic - what data do pharma need in order to become interested?	1. Develop new leaders in the field a. Consider design of an international trial that has potential for different / new treatments and possibility to can add new treatments 2. TKIs – good phase II evidence provides potential for a trial, but not clear which one? Several surgical questions to be asked. ICONIC could provide platform for these questions and also RT questions. a. Use ICONIC as a platform to ask surgical questions and RT questions. 3. International trial has been done before - hard but possible. Keen for international collaboration a. Liaise with international osteosarcoma groups to design / contribute to an international trial.

	b. Employ a dedicated person to introduce international trials and open these in the UK 4. Could invite pharma to meetings →ACTIONS • Arrange a sandpit style meeting to plan potential studies • Work with NCRI Sarcoma Research Group and the bone subgroup to develop follow-on therapeutic clinical trials. Add this to the agenda a. Ensure correlative/ translational questions b. Explore membership of bone subgroup? Opportunity for greater translational, clinical scientific input. Email chair of this group. c. Opportunities to optimise the use of imaging for osteosarcoma to improve surgery d. Biomarker discovery – should be included in trial design
4. Communication	
1. Little oversight/knowledge of what is happening and who is doing what. a. Where do skills/models/tools exist. b. **limited oversight as to what is happening internationally**	1. Develop an osteosarcoma consortium / hub ○ dedicated person/people to run this ○ website to keep list of skills/expertise ○ have working groups - with leads for each ○ link to current structures such as GeCIP, ORC, ICONIC ○ Charity involvement ○ Link with the NCRI Sarcoma Research Group and other relevant NCRI research groups

c. **Do not consistently feed issues / problems back or things that** have not been successful. This is equally important to inform the community so people don't make same mistakes 2. Networking between different fields/expertise not done. Meetings usually clinical or basic science focussed and lacking a meeting for everyone to come and share knowledge **Example: many delegates not aware of other consortia such as GeCIP and what it wants to achieve?** 3. Lack of osteosarcoma cellular and mouse models – what models are available across the community	○ Any hub or consortium should be transparent and open - bringing everyone together with no bias towards one area/focus a. Map of who current researchers are and their skills/expertise b. Link to international research Promote sharing of negative results and issues/problem solving 2. Repeat symposium at least annually ○ Invite clinicians, scientists and other stakeholders identified in skills gap analysis *Requires defined output with actions w community can work in a more collaborative way and move away from silo working.* ○ Develop link with aligned research groups such as GeCIP and disseminate updates 3. Map current pre-clinical models and where these are available. →ACTIONS 1. Explore the development of an Osteosarcoma consortium / hub 2. Secure funding to repeat the Symposium annually 3. i) Map models used by researchers and opportunities to share these or develop collaborations ii) Charities to hold specific calls to develop models of osteosarcoma and for these to be open for use by wider community

5. Data	
1. Data collected in clinical research isn't consistent and is often vague therefore hard to link to research	1. ICONIC may solve this? a. Standardise systems and data. b. Work collaboratively with the international osteosarcoma community - data harmonisation project. Identify person to lead on this.
2. NCRAS data - problems accessing this, sarcoma data completeness for basic fields is poor and does not capture all information such as relapse and outcomes	2. Develop better links to NCRAS to use data more effectively and capture new/important fields not currently captured c. Charities to engage with NCRAS to improve data collection. ACTION → SS to ask BCRT for a letter of support for this.
3. What clinical data is being collected as part of GeCIP and how can it be accessed?	3. Develop better links with GeCIP a. Invite community to GeCIP meetings and advertise access requirements
6. Infrastructure & current practice	
1. Consent processes outdated and laborious	*1. There is not much we can do about this*
2. Not clear how sequencing will become standard of care and be embedded in to NHS	2. Build on existing initiatives: • Scope the possibility of increased infrastructure grants to support sample collection for this sequencing • Engage with NHS England and share information on this – communicate via hub/consortium • Align with other research projects including SM Paeds
3. continued issues with accessing patient material a. especially for researchers outside of the 5 surgical centres. b. Little understanding of use of tissues / the need generally	3. Should we be standardising practice? Particularly around samples for research, data collection, consent. Harmonise SOPs and data collection where possible – develop a minimum dataset.

4. Research infrastructure not embedded in to NHS	4. Could we link with current initiative - use the UK CRC tissue directory to map samples and processes for applying for using samples a. All centres to sign up to the UKCRC directory Database of clinical b. Transparent access policies and procedures from each of the bone centres → ACTIONS BCRT to ensure that infrastructure grant information is accessible on the website, detailing contacts and access policies. Biobanks at surgical centres are linking with UKCRC Tissue Directory – BCRT to ensure a network is developed and is communicated on the BCRT website and any hub/consortium.
7. Awareness initiatives	
1. Lack of awareness of osteosarcoma amongst public/GPs/Allied Healthcare Professionals a. Delay in diagnosis major challenge	1. E-modules currently exist, can these be utilised/maximised/improved? a. Funding for projects –aligned to ongoing initiatives where possible b. Charities to work together to identify specific issues and priorities c. Link with Living with and beyond cancer and other initiatives d. Work with GPs and physiotherapists ACTIONS→ Assess what is currently available and develop a plan / application for funding to address awareness and delay in diagnosis