Report

Intergroup bone sarcoma networking meeting within ECT-EUROCORES

2nd International Meeting on Future Clinical Trials for the Adjuvant Treatment of Osteosarcoma: Creating a Strategic Consensus

London, UK; 27.-28.02.2012

Summary and scientific content:

Background:

This meeting was held as joint meeting of the Pan European Clinical Trials (ECT) – EUROCORES / European and American Osteosarcoma Study EURAMOS, the German GPOH Cooperative Osteosarcoma Study Group (COSS) and the EUROPEAN NETWORK for CANCER research in CHILDREN and ADOLESCENTS (ENCCA) - Workpackage 7 (Integrating clinical trials and tumor biology research in bone sarcoma) on the subject of networking between the most common bone cancer but still orphan disease in children and adolescents: Osteosarcoma. Meeting organizers were Jeremy Whelan (EOI), representing EURAMOS and ENCCA Work Package 7.3 (Developing a European platform for clinical trials in osteosarcoma).

Proceedings of the Meeting

While the groups collaborating in European bone sarcoma trials have found solutions for many challenges posed for successful recruitment and the day-to-day management of a complex multinational trial infrastructure, the implementation of integrated biology studies remains challenging. While several projects work successfully, for instance the collaboration

between the osteosarcoma platform of the rare disease network “EUROPEAN NETWORK for CANCER research in CHILDREN and ADOLESCENTS” (ENCCA) and European EURAMOS-investigators, there is still ample room for improvement and for implementation of collateral studies on a larger scale. In order to accomplish this for the osteosarcoma, the ECT-EURAMOS group intends to link with and join forces with the established Network of Excellence formed within the European Union´s Framework Program 7 – ENCCA.

Delegates from ECT-EURAMOS representing the Cooperative Osteosarcoma Study Group (COSS), the European Osteosarcoma Intergroup (EOI), the North American Children´s Oncology Group (COG) and the Scandinavian Sarcoma Group (SSG). Investigators from other bone sarcoma groups who have formed European Networks of Excellence: ENCCA (EUROPEAN NETWORK for CANCER research in CHILDREN and ADOLESCENTS) Workpackage 7 and leading representatives from other bone tumor and biology groups: the Italian Sarcoma Group (ISG), the Australasian Sarcoma Study Group (ASSG), SARC, GEIS, the Société Française de Lutte contre les Cancers et Leucémies de l'Enfant et de l'Adolescent / Groupe Sarcomes Français et Groupe d'Etude de Tumeurs Osseuses (SFCE/GETO) and CRUK joined the meeting.

The aim of the meeting was to provide a forum for broad-based discussion by key stakeholders regarding the role of osteosarcoma treatment and research, including pediatric and medical oncology, pathology, radiology, orthopedic and thoracic surgery, radiotherapy, biometrics, and tumor biology. 34 participants take part per day from 13 countries: Australia (N=1), Austria (N=1), Denmark (N=1), France (N=1), Germany (N=5), Italy (N=2), Norway (N=1), Spain (N=2), Sweden (N=1), Switzerland (N=1), The Netherlands (N=2), United Kingdom (N=7) and USA (N=9) have taken part.

Challenges to successful treatment and research

We reviewed the experience of different specialists from different groups, to see what could be learnt for the future. More detailed information is included in the minutes of the meeting. The challenges and obstacles faced in recent EURAMOS-1 study as well as in research consortiums, were defined point by point. Successful solutions which were identified during these projects were forwarded into a coordinated intergroup strategy. The intergroup trial consortium was confirmed. Study results and what we have learned from EURAMOS-1 was presented and discussed. A review of current trial activities was presented and priorities for trial development and for a clinical translational research strategy discussed. In addition strategies were discussed for the topics current international standard of care for randomized trials with newly diagnosed osteosarcoma and relapsed disease. A consensus was reached for standardizing study design for eligibility criteria and outcome measures. The meeting

included investigators from over a dozen European countries who will in turn disseminate the content and spirit of the meeting to their responsible organizations and to act as a forum to motivate investigators from all countries to continue coordinated translational research activities for bone sarcoma biology.

Conclusion

The meeting of the international EURAMOS group with their partners from all over Europe and from overseas provided an interdisciplinary forum for the advancement of translational and clinical research proposals into Pan-European osteosarcoma trials. Following up on previous meetings held within the ECT-framework and building on the experience of the ECT-EURAMOS trial, intergroup collaboration for osteosarcoma was strengthened.

Number of participants: 34 (32 each day)

Countries: 13

Australia (N=1), Austria (N=1), Denmark (N=1), France (N=1), Germany (N=5), Italy (N=2), Norway (N=1), Spain (N=2), Sweden (N=1), Switzerland (N=1), The Netherlands (N=2), United Kingdom (N=7), USA (N=9).

Assessment of the results and impact of the event on the EUROCORES Programme:

The aim of the meeting was a networking meeting, to provide a forum for broad-based discussion by key stakeholders regarding the optimizing of treatment recommendations and for developing translational research and new study proposals for osteosarcoma.

Prof. Dr. Stefan Bielack	**Dr. Miriam Wilhelm**	**Christina Döringer**
ECT-EURAMOS, Project leader	COSS study physician	Authorized financial officer
ENCCA WP7 leader / Applicant		

Annexes:

- Financial report
- Agenda (final)
- Minutes
- List of participants

Detailed report of Expenditures

Accommodation (from February 26 – 27 and/or 27 - 28, 2012):	
Prof. Dr. Stefan Bielack (26/02/2012; Accommodation)	€ 314.29
Dr. Laurence Brugières (20/02/2012; Accommodation)	€ 111.33
Dr. Mikael Eriksson (28/02/2012; Accommodation)	€ 318.11
Prof. Leo Kager (28/02/2012; Accommodation)	€ 310.05
Dr. Catherine Rechnitzer (28/02/2012; Accommodation)	€ 311.47
Kirsten Sundby Hall MD, PhD (28/02/2012; Accommodation)	€ 311.47
Dr. Miriam Wilhelm (27/02/2012; Apartement)	€ 153.48
Total	**€ 1,830.20**
Travel:	
Dr. Daniel Baumhoer	€ 188.09
Prof. Dr. Stefan Bielack	€ 206.00
Dr. Laurence Brugières	€ 129.00
Dr. Gabriele Calaminus	€ 232.95
Anne-Marie, Cleton-Jansen, PhD	€ 283.93
Dr. Mikael Eriksson	€ 173.80
Prof. Leo Kager	€ 398.73
Kirsten Sundby Hall MD, PhD	€ 406.32
Dr. Miriam Wilhelm	€ 156.61
Total	**€ 2,175.43**
Grant Total	**€ 4,005.63**
Requested Funding	**€ 5,000.00**
Funding from ESF-Foundation (80% from requested funding)	**€ 4,000.00**
Expenditures	**€ 4,005.63**
Not used Grant	**€ 994.37**
Remittances from ESF requested	**€ -05.63**

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2nd International Meeting on Future Clinical Trials for the Adjuvant Treatment of Osteosarcoma: Creating a Strategic Consensus

27th and 28th February 2012, London UK

Meeting Report for ESF - FINAL

GROUP	ATTENDEES
EOI	Jeremy Whelan (Chair), Matthew Sydes, Hans Gelderblom, Anne-Marie Cleton-Jansen, Sandra Strauss, Rachael Windsor
COG	Neyssa Marina (Co-chair), Richard Gorlick, Holcombe Grier, Mark Krailo, Katie Janeway, Michael Isakoff, Rob Goldsby
SSG	Kirsten Sundby Hall, Catherine Rechnitzer, Mikael Eriksson
COSS	Stefan Bielack, Leo Kager, Michaela Nathrath, Daniel Baumhoer, Miriam Wilhelm, Gabriele Calaminus, Attyla Drabik
ISG	Stefano Ferrari, Franca Fagioli
ASSG	David Thomas
SARC	Denise Reinke, Larry Baker
GEIS	Javier Martin Broto, Oscar Gallego
SFCE/GETO	Laurence Brugières
CRUK	Nicola Keat
Observers	MRC: Jane Hook, Gordana Jovic

BACKGROUND

A 2-day meeting was held in London on 27-28th February 2012 with the aim of agreeing a co-ordinated programme of clinical research in osteosarcoma under the auspices of the EURAMOS group.

Osteosarcoma is a rare cancer with a peak incidence in adolescence, but also affects younger children and adults. There has been no clinically significant improvement in survival for over 20 years. The reasons behind this are multi-factorial but include fragmentation of clinical research; historically, there has been a lack of randomised controlled trials and an over-reliance on single arm studies. RCTs that have been conducted have either been small or have had long recruitment periods. Furthermore, heterogeneity in eligibility criteria, data collected and outcome measures used in trials from different research groups has limited the interpretation of cross-trial evidence. This is in common with challenges that beset research in other rare cancers. An additional challenge in osteosarcoma is the age group affected, necessitating co-operation between paediatric and adult oncology.

The original EURAMOS (European and American Osteosarcoma Studies) group was a trans-Atlantic collaboration formed between the European Osteosarcoma Intergroup (EOI), Cooperative Osteosarcoma Studies group (COSS) and Scandinavian Sarcoma Group (SSG) in Europe, and the Children's Oncology Group (COG) in the USA. The first trial from the EURAMOS group, EURAMOS-1, a randomised phase III trial investigating risk-stratification in the adjuvant treatment of newly diagnosed osteosarcoma, has recently completed recruitment with 2260 patients with localised or resectable metastatic disease registered over a period of 6 years (2005-2011). It is the largest trial yet conducted in osteosarcoma.

Following demonstration of the feasibility of this broad international collaborative approach through EURAMOS-1, EURAMOS has expanded to include most of the other leading global osteosarcoma research groups: ISG, GEIS, SFCE-GETO, ASSG, SARC and the EORTC. An executive body, the EURAMOS Strategy Group (ESG), with representation from each constituent group was formed in 2010 and meets regularly by teleconference; it also met in person at ASCO 2011. An initial trial-planning meeting was held in 2010 (the 1st International Meeting on Future Clinical Trials for the Adjuvant Treatment of Osteosarcoma: Prioritising the Questions, 15-16th March 2010, London). The consensus from that meeting was to develop a follow-on phase III RCT in the adjuvant setting. The priority questions requiring investigation were agreed as (i) to further investigate the efficacy of mifamurtide; (ii) to investigate the efficacy of bisphosphonates in addition to adjuvant chemotherapy; and (iii) to standardise the chemotherapy backbone of treatment. Development of a trial including mifamurtide was attempted but was not possible due to lack of relevant industry support. A trial proposal investigating the addition of zoledronic acid (ZA) to MAP chemotherapy (EURAMOS-2) in patients <65 years with localised, resectable or unresectable metastatic osteosarcoma was developed with COG as the lead group, but did not achieve the support of COG Scientific Council at peer review. In acknowledgment of a need to review the priorities set in 2010, this meeting was called.

Funding for this meeting was provided by the European Science Foundation via its EUROCORES programme and the European Network for Cancer Research in Children and Adolescents (EU FP7 Network of Excellence). Organisational support was provided by the MRC and Cancer Research UK.

MEETING AIMS

This meeting was conceived with the aim of agreeing a co-ordinated research programme to

support the development of an international clinical trial in patients with newly diagnosed osteosarcoma using a multi-arm multi-stage (MAMS) design. The MAMS design is a phase II/III trial that permits simultaneous evaluation of multiple investigational agents and allows early identification of insufficiently active interventions in the context of a single protocol; developing a MAMS trial would employ modern, efficient clinical trial design in the setting of a rare cancer. In order to lay the foundations for a MAMS (or other methodologically innovative) trial in the adjuvant setting in the future, we aimed to address and reach consensus on questions fundamental to developing a productive period of research in osteosarcoma. The themes addressed were:

1. Reflection on lessons learned from EURAMOS-1 and attempts to develop EURAMOS-2
2. Standardising clinical trials in osteosarcoma
3. Identifying priority agents for clinical testing and translational research priorities
4. Agreeing a strategic direction and programme of activities

MEETING FORMAT

The ESG lead from each constituent group was asked to nominate attendees to represent their group. The expertise of attendees included adult and paediatric oncology, trial management, biostatistics, pathology and basic/translational science. A representative from Cancer Research UK was invited to give a funder's perspective on research in rare cancers and information on the International Rare Cancers Initiative (IRCI). Representatives from European-based consumer groups were invited but were unable to attend.

Prior to the meeting, each group lead was asked to complete questionnaires detailing clinical trials ongoing or in development in their group, and to identify targeted agents and biomarkers they considered to be of potential interest in osteosarcoma. These questionnaires were used in the development of the agenda and circulated to attendees to inform group discussion during the meeting.

The meeting was organised as a combination of development and consensus sessions (Appendix 1 – Agenda). The development sessions were designed to provide background for the consensus discussions through presentation of responses to the pre-meeting questionnaires and reflection on past EURAMOS activities. All groups presented information on their ongoing trials and trials-in-development or proposals for future trials. The aims of the consensus sessions were to agree a position on questions important to the development of a group clinical research strategy; and in the final session to agree a plan to develop a co-ordinated programme of clinical trials. Slides from the meeting presentations are available via the EURAMOS website (www.euramos.org).

DISCUSSIONS

1. Reflection on experience gained from past activities

- There was general consensus that participating in EURAMOS-1 has been a positive experience for the groups involved and demonstrates that international collaboration is feasible. There was considerable enthusiasm from all groups to maintain and develop the EURAMOS group.
- There are organisational procedures that could be refined in future trials, particularly around the structure of data collection. It was felt that in future collaborative trials, a single trial database reflecting a unified approach to data collection with capabilities for remote data entry would simplify trial procedures.
- Managing biological sample collection and co-ordinating associated biological studies has also been challenging in the context of a multi-national trial. The role of virtual

biobanks was discussed. For COG, having a single trial biobank for patients from the USA works well; in Europe, however, where patients are recruited from many countries, it is not feasible to centrally store samples from all patients. Establishment of the EuroBoNet network has facilitated translational research for its participants. The importance of robust quality control and assurance was agreed by all. Trial sample collection and the structure of collaborative translational research requires further specialist consideration and the EURAMOS translational studies group is already established.

- It was agreed that international co-ordination is essential to improve outcomes given the limited number of patients with osteosarcoma, to make clinical research more efficient and to avoid duplication. However, there are significant logistic and bureaucratic hurdles to overcome in a EURAMOS-1-type collaborative trial; and it may not always be the most appropriate model for collaboration. Alternative models may include:
    - a series of phase II trials conducted by a limited number of groups or in parallel in different groups
    - smaller phase III trials that involve some, but not necessarily all, groups
- There is significant pressure for limited resources from funding bodies; and there is a need for a strong scientific rationale for an intervention and supporting clinical data providing preliminary evidence of activity before more conservative funders will commit to funding a phase III trial.
- Key questions that have arisen out of our experience with EURAMOS-2 are:
    - What supporting evidence do we need to satisfy funding bodies?
    - How do we go about getting that evidence?
    - What are the components of study design – inclusion criteria and outcome measures - that will deliver the information required?
    - Can we engage with funding bodies to attempt to streamline the peer review process across multiple countries?
- The importance of engaging with funding bodies when planning trials was agreed. Even though we have demonstrated that we can collaborate successfully the challenges in conducting clinical trials in osteosarcoma have not diminished and we face many of the same barriers that less established groups in other rare cancers face. Support from initiatives like the IRCI could help us to overcome these barriers, in particular in facilitating collaborations with industry and in streamlining the requirements for peer-review by multiple national funding bodies.

2. Standardising clinical trials in osteosarcoma

i. Phase II trials

- The role of phase II trials, both single-arm and randomised, in assessing the activity of targeted therapies was discussed. Historically, heterogeneity in eligibility criteria and outcome measures used has limited the clinical impact of these trials.
- It was agreed that a EURAMOS-wide phase II trial is not feasible and would introduce disproportionate regulatory and financial barriers. Group-specific, or limited international, trials with co-operation in planning and data-sharing via the ESG would be feasible and maximise efficiency. This could be achieved by trial proposals being presented at ESG meetings with regular progress updates thereafter.
- Efforts should be made to standardise eligibility criteria and the outcome measures used.
- Trial designs were discussed. It was agreed that either single-arm or randomised designs may be appropriate, although it should be acknowledged that only randomised data is likely to lead to a change in clinical practice. The choice of design and eligibility criteria depend on trial-specific factors, e.g. the agent being tested and

the population involved.
- A minimum common data-set of baseline demographic data to be collected should be defined for use on a group-wide basis.
- The most informative outcome measures are likely to be progression-free survival in randomised trials and clinical benefit rate in single-arm studies. The optimal time-point to be used for assessment of clinical benefit rate is undefined.
- It was agreed that defining acceptable criteria for standardisation of phase II trials conducted by member groups should be a priority for the ESG to ensure that results obtained are fit-for-purpose, i.e. provide clinically useful information that can rapidly and reliably identify agents with evidence of activity and inform the development of future phase III trials.

ii. Phase III trials

- Appropriate eligibility criteria and outcome measures for future adjuvant phase III trials were discussed in terms of broad principles.
- It was agreed that the criteria used in EURAMOS-1 should form the basis of those used in future trials. The principle of having broad eligibility criteria, e.g. to include patients aged >40 years and those with more extensive metastatic disease, was generally supported on the basis of giving previously excluded patients access to treatment on clinical trials where feasible. However, the implication of introducing greater heterogeneity into a trial population will require specific consideration during the design process.
- Event free survival remains an appropriate primary outcome measure, with overall survival as a secondary outcome. In general, assessment of patient reported outcome measures should be included.
- To improve trial efficiency, where sufficient early phase clinical data exists, it would be desirable to design phase III trials with an embedded phase II (activity) stage rather than performing separate phase II and III trials.

iii. Comparator arms

- Definition of a single acceptable chemotherapy regimen for use as a comparator arm in adjuvant trials is limited by the lack of head-to-head comparisons between regimens currently in use in standard clinical practice.
    - Despite this, the weight of evidence suggests that 3- or 4-drug regimens are more effective than 2-drug regimens
    - Areas of contention remain around:
        - whether the addition of ifosfamide to methotrexate, doxorubicin and cisplatin (MAP)-containing regimens confers increased efficacy
        - the efficacy of non-doxorubicin-containing regimens, which are considered standard treatment in France and form the comparator arm in the current SFCE-GETO study of chemo +/- zoledronic acid.
        - the role of mifamurtide, which is licensed for use by the EMA but not the FDA
    - There was general (but not universal) agreement that MAP, as used in EURAMOS-1, remains the group's preferred comparator. This may change depending on the results of EURAMOS-1 in due course.
    - Mifamurtide was agreed to remain a priority agent for further investigation in the context of clinical trials. However, the differential availability of the drug across participant countries and pressures for its use as part of standard clinical care in some of these countries may continue to prevent future co-operative trials.
    - It was agreed that a EURAMOS-wide retrospective pooled individual patient data (IPD) analysis looking at outcomes by treatment regimen, although

complex to perform and interpret, may be informative in determining the relative efficacy of the different standard chemotherapy regimens in use. A trial directly comparing chemotherapy regimens is now unlikely to ever be performed. Instead, we need to concentrate efforts on defining an acceptable chemotherapy backbone to be used in future trials of chemo +/ targeted therapy.

- Trials of chemotherapy in the setting of recurrent disease were also discussed. It was agreed that there is no standard of care for resectable recurrent osteosarcoma.

3. Identifying priority agents for clinical testing & translational research priorities

- The available evidence for different targeted therapies identified as being of potential interest from the pre-meeting questionnaires was presented and discussed. These agents can be divided into those for which there is (i) some osteosarcoma-specific clinical data already available: mifamurtide, inconclusive efficacy data from INT0133 trial; zoledronic acid, feasibility only; and multi-targeted TKIs and mTOR inhibitors, limited data; and (ii) pre-clinical evidence only, e.g. RANK-ligand-targeted therapy; Alk/Met, Hedgehog pathway, Src kinase inhibition; anti-CTLA4 and GD2 antibody immunotherapy.
- Currently, the only agents with sufficient evidence to justify embarking on a phase III trial are mifamurtide and zoledronic acid.
- It was agreed that the most compelling agent for testing remains mifamurtide. A trial proposal was presented by the COSS group but there remain significant unknowns including the availability of industry support, without which the trial could not be conducted in countries outside of the EU and is unlikely to be feasible even in Europe.
- SFCE/GETO have an ongoing phase III trial investigating the addition of zoledronic acid to standard chemotherapy in the adjuvant setting.
- There are no compelling clinical data for any other targeted agents at the moment but there are a number of promising targets and the evaluation of these agents in phase I/II trials should be optimised.
- The use of correlative science via integrated translational studies in early phase clinical trials will be critical in providing supportive evidence for the rationale of taking agents forward into late phase trials in the adjuvant setting.

4. Agreeing a co-ordinated programme of clinical research

- It was agreed by all that international co-operation in osteosarcoma clinical research is both necessary and feasible.
- Currently, a multi-arm multi-stage trial in first-line therapy is not suitable.
    - There are outstanding questions related to the efficacy of mifamurtide and zoledronic acid
    - A number of promising molecular targets have been identified but no compelling clinical data for any targeted agents is yet available
- The ESG should focus on optimising the evaluation of novel (in the context of osteosarcoma) therapies with the aim of generating timely, reliable evidence of clinical activity to inform the development of a future phase III trial investigating the efficacy of targeted therapies in the adjuvant setting.
- This will be achieved by developing a series of co-ordinated early phase trials in member groups, which will require:
    - Communication between groups, via the ESG, to ensure non-overlapping studies
    - Definition of a set of standards for phase II trials in osteosarcoma covering

trial design and procedures, eligibility criteria, outcome measures, data collection and procedures for data-sharing between EURAMOS member groups via the ESG.

- EURAMOS can continue without a group-wide phase III trial. Individual member groups who are willing/able to do so may chose to join the ongoing SFCE-GETO zoledronic acid trial and/or participate in developing a proposed mifamurtide trial (Figure 1).
- Involvement with consumer groups should be developed further, to increase their input in trial development and conduct.
- The ESG should continue to engage with industry and funding bodies, and lobby for the inclusion of osteosarcoma in initiatives to support research in rare cancers.

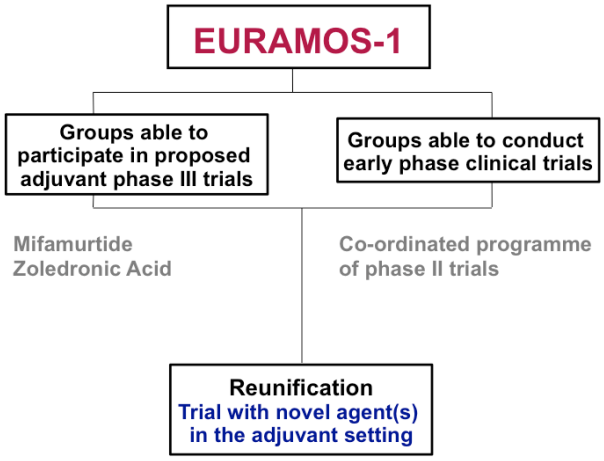

Figure 1. Proposed EURAMOS research programme

OUTCOMES & ACTIONS

- A follow-on meeting to develop consensus standards for phase II trials is to be held at ASCO 2012. Supportive actions include groups reviewing their data on outcomes in relapsed osteosarcoma to determine a single appropriate timepoint for assessment of clinical benefit rate.
- Development of proposals for a mifamurtide trial.
- Development of proposals for a retrospective IPD analysis of outcome by chemotherapy regimen.
- Groups to consider participation in the French-led zoledronic acid trial.
- The ESG will continue to meet regularly by teleconference and annually in person at CTOS. An in-person meeting will be organised during CTOS 2012.

Appendix 1 – Meeting Agenda

2nd International Meeting on Future Clinical Trials for the Adjuvant Treatment of Osteosarcoma: Creating a Strategic Consensus

Royal Institute of British Architects, 66 Portland Place, London W1B 1AD
27th and 28th February 2012

AGENDA

Meeting aim: To agree a co-ordinated research program to support the development of an international multi-arm multi-stage clinical trial in patients with newly diagnosed osteosarcoma.

Group	Attendees
EOI	Jeremy Whelan*, Matthew Sydes*, Hans Gelderblom*, Anne-Marie Cleton-Jansen*, Sandra Strauss*, Rachael Windsor
COG	Richard Gorlick, Neyssa Marina*, Holcombe Grier*, Mark Krailo*, Katie Janeway*, Michael Isakoff*, Richard Goldsby*
SSG	Kirsten Sundby Hall*, Catherine Rechnitzer, Mikael Eriksson*
COSS	Stefan Bielack*, Leo Kager*, Michaela Nathrath, Daniel Baumhoer*, Miriam Wilhelm, Gabriele Calaminus*, Attyla Drabik
ISG	Stefano Ferrari*, Franca Fagioli
ASSG	David Thomas*
SARC	Denise Reinke*, Larry Baker
GEIS	Javier Martin Broto*, Oscar Gallego
SFCE/GETO	Laurence Brugieres*
CRUK	Nicola Keat*
Others	MRC: Jane Hook*, Gordana Jovic

** Included as session chair, discussant, rapporteur or presenter – please check agenda for role and notes below for instructions*

Meeting format & roles of participants:

Combination of (i) consensus sessions and (ii) development sessions.

1. Consensus sessions

The aim of the consensus sessions is to agree a position on several questions important to the development of a clinical research strategy. A planned output of the meeting is to publish these as a consensus statement on clinical trials in osteosarcoma/strategic goals of the EURAMOS Strategy Group (ESG).

We have nominated a discussant and rapporteur for each of these sessions.

- We request discussants to prepare a 5-10 minute presentation to set the background to the agenda topic keeping in mind the principal goal of the meeting, to reach a consensus on strategy for trials.
- The role of the rapporteur is to lead the response to the presentation, draw threads together, ensure all aspects are covered, and that other groups and individuals are heard during the session. They are also responsible for leading the write-up of the session after the meeting.
- The role of the session chair is to oversee proceedings, and encourage discussion and consensus.

2. Development sessions

The aim of these sessions is to provide background for the consensus discussions through presentation of responses to the pre-meeting questionnaires and reflection on past EURAMOS activities.

We have nominated a session chair and presenters for these sessions.

- The role of the session chair is to co-ordinate presentations, facilitate group discussion, draw threads together and ensure all relevant aspects covered.
- The role of the named presenters is to give a short presentation on the topic indicated.

SESSION INFORMATION		LEAD PARTICIPANTS
Monday 27th February		
0915 – 1000	**Registration**	
SESSION 1	**Chair: Jeremy Whelan**	
1000 – 1020	**Welcome and introduction** - Identifying a strategy for clinical research: o Meeting aims o Consensus o Representation from groups and other stakeholders o Consumer involvement in planning research in osteosarcoma	
1020 - 1100	**What have we learnt from attempting to develop a ZA trial?** [Development session] o Peer reviewers requirements o Funders needs & perspectives on research in rare cancers – the International Rare Cancers Initiative	**Presenters:** Mike Isakoff Nicola Keat
1100 – 1230	**Where are we now?** [Consensus session] - Current international standards of care, i.e. what are acceptable standard arms for randomised trials in patients with: o Newly diagnosed osteosarcoma o Relapsed disease	**Discussant:** Neyssa Marina **Rapporteur:** Hans Gelderblom
1230 - 1330	*LUNCH*	
SESSION 2	**Chair: Stefan Bielack**	
1330 – 1500	**Reaching a consensus on standardising study design** [Consensus session] - Eligibility criteria and outcome measures o Newly diagnosed ▪ Which patients should be included? • Age limits • Metastatic disease ▪ What are the most appropriate outcome measures? o Relapsed disease ▪ Which patients should be included? ▪ What outcome measures are we and should we be using?	**Discussants:** Stefano Ferrari (elig) Mark Krailo (OM) **Rapporteurs:** Mikael Eriksson (elig) Denise Reinke (OM)/TBC
1500 – 1530	*TEA*	

SESSION INFORMATION		LEAD PARTICIPANTS

1530 – 1800	**What are the addressable questions? (part 1)**
	Review of current trial activity and priorities for trial development identified from national group questionnaires [Development session]
	
	- Presentation of open trials/proposals – 1st line phase III (max. 10 mins/presentation)
	  ○ SFCE/GETO – Zoledronic acid
	  ○ COSS – MTP trial
	  ▪ Quality of Life
	  ▪ TR sub-study
	
	- Presentation of trials open/in development/proposals - other (max.10 mins/presentation)
	
	- Other agents of interest identified from questionnaires
		Presenters:
		Group representatives*
		
		Laurence Brugieres COSS
		
		EOI, COG, SSG, ISG, ASSG, SARC, GEIS group representatives
		
		Jane Hook

**Groups to determine their own presenters*		

SESSION INFORMATION		LEAD PARTICIPANTS
Tuesday 28th February		
SESSION 3	**Chair: Holcombe Grier**	
0830 – 0945	**What have we learned from EURAMOS-1? (and what could we do better)** [Development session] ~10 mins each on: - Infrastructure - Biological studies - Perspective from PI - Perspective from investigator – USA - Europe - Perspective from non-participant	**Presenters:** Matt Sydes A-M Cleton-Jansen Stefan Bielack Rob Goldsby Kirsten Sundby Hall David Thomas
0945 – 1000	*TEA*	

1000 – 1115	**Biology and pathology - EURAMOS Translational Studies Group** [Consensus session] - Identifying translational research priorities and promising biomarkers - Practical considerations for collaboration	**Discussant:** David Thomas **Rapporteur:** Javier Martin
1115 – 1130	*TEA*	
1130 – 1300	**What are the addressable questions? (part 2)** [Consensus session] - Reaching a consensus on priority agents for clinical testing o Building on presentations and discussion from 27th Feb	**Discussant:** Katie Janeway **Rapporteur:** Leo Kager
1300-1400	*LUNCH*	
SESSION 4	**Chair: Jeremy Whelan**	
1400 – 1615	**Setting a global plan** [Consensus session] - Agreeing a co-ordinated clinical trial programme - Strategic goals of ESG	All
1615 – 1630	*TEA*	
1630 – 1700	**Moving forward** - Concluding remarks	Jeremy Whelan Neyssa Marina

2nd International Meeting on Future Clinical Trials for the Adjuvant Treatment of Osteosarcoma: Creating a Strategic Consensus

London, UK, 27th and 28th February 2012

Participants list

Title	Name	First name	Sex	Group	Affiliation	Address	Email-Address	Telephone number	Fax number
Prof.	Baker	Laurence (Larry)	M	SARC	University of Michigan, Medical School	24 Frank Lloyd Wright. Dr PO Box 483 Ann Arbor MI 48106 USA	bakerl@umich.edu	+1 734 998 7130	+1 734 998 7118
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Prof. Dr.	Bielack	Stefan	M	COSS	Klinikum Stuttgart - Zentrum für Kinder- und Jugendmedizin – Olgahospital	Bismarckstr. 8 70176 Stuttgart Germany	S.Bielack@klinikum-stuttgart.de	+49 (0) 71127872460/1	+49 (0) 71127872462
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PD Dr.	Nathrath	Michaela	F	COSS	Klinikum Kassel Pädiatrische Hämatologie und Onkologie	Mönchbergstr. 41 34125 Kassel Germany	michaela.nathrath@klinikum-kassel.de michaela.nathrath@me.com	+49 (0) 5619803379	+49 (0) 5619806813
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2nd International Meeting on Future Clinical Trials for the Adjuvant Treatment of Osteosarcoma: Creating a Strategic Consensus

London, UK, 27th and 28th February 2012

ATTENDANCE LIST

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Nr	*Family Name*	*First Name*	*Affiliation*	*Signature*
1	Larry	Baker	SARC	
2	Baumhoer	Daniel	COSS	
3	Bielack	Stefan	COSS	
4	Brugières	Laurence	SFCE/GETO	
5	Calaminus	Gabriele	Univ. Hosp. Muenster	
6	Cleton-Jansen	Anne-Marie	EOI	
7	Drabik	Attyla	Univ Hosp Muenster - EURAMOS Intergroup Safety Desk	
8	Eriksson	Mikael	SSG	
9	Fagioli	Franca	Italian Sarcoma Group	
10	Ferrari	Stefano	Italian Sarcoma Group	

Meeting Secretary (name and signature): ……

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12	Gelderblom	Hans	EOI	
13	Goldsby	~~Richard~~ Robert	COG	
14	Gorlick	Richard	COG	
15	Grier	Holcombe	COG	
16	Hook	Jane	MRC	
17	Isakoff	Michael	COG	
18	Janeway	Katie	COG	
19	Jovic	Gordana	MRC	
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22	Krailo	Mark	COG	
23	Marina	Neyssa	COG	
24	Marreaud	Sandrine	EORTC	
25	Martin Broto	Javier	GEIS	
26	Nathrath	Michaela	COSS	
27	Rechnitzer	Catherine	SSG	
28	Redondo	Andrés	GEIS	
29	Reinke	Denise	SARC	
30	Sundby Hall	Kirsten	SSG	

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Nr	*Family Name*	*First Name*	*Affiliation*	*Signature*
31	Sydes	Matthew	EOI	
32	Thomas	David	ASSG	
33	Whelan	Jeremy	EOI	
34	Wilhelm	Miriam	COSS	
35				
36				
37				
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Nr	*Family Name*	*First Name*	*Affiliation*	*Signature*
41	Strauss	Sandra	EOI	
42				
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6	Cleton-Jansen	Anne-Marie	EOI	
7	Drabik	Attyla	Univ Hosp Muenster - EURAMOS Intergroup Safety Desk	
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25	Martin Broto	Javier	GEIS	
26	Nathrath	Michaela	COSS	
27	Rechnitzer	Catherine	SSG	
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