Area for consideration		Response
1. Trial		
1.1	Short name or acronym	**EURAMOS-1**
1.2	Trials Unit	MRC Clinical Trials Unit
1.3	Full descriptive name of trial	A randomized trial of the European and American Osteosarcoma Study Group to optimize treatment strategies for resectable osteosarcoma based on histological response to pre-operative chemotherapy
1.4	Sponsor	Medical Research Council
1.5	IMP trial?	Yes
2. Trial reference numbers		
2.1	ISRCTN	ISRCTN67613327
2.2	NCT	NCT00134030
2.3	EUDRACT No	2004-000242-20
2.4	Funding UK	Cancer Research UK & MRC
2.5	Others	Europe ESF (European Science Foundation) (Ref No MM/NG/EMRC/0202) Belgium FNRS (Fonds National de la Recherche Scientifique) Belgium FWO (Fonds voor Wetenschappelijk Onderzoek-Vlaanderen) Canada Children's Oncology Group Denmark Danish Medical Research Council Finland Academy of Finland Germany DFG ref No: BI 1045/1-1 & 1-2 Germany DKH ref No: 50-2723-Bi2 Hungary Semelweis Foundation Netherlands ZonMw (Council for Medical Research) Norway Research Council of Norway Sweden Scandinavian Sarcoma Group Switzerland Swiss Paediatric Oncology Group (SPOG) USA Children's Oncology Group
3. Lead researchers, including Coordinating Data Centre[1]		
3.1	Chief Investigator(s)	Stefan Bielack, Cooperative Osteosarcoma Study Group (COSS) Jeremy Whelan, European Osteosarcoma Intergroup (EOI) Sigbjørn Smeland, Scandinavian Sarcoma Group (SSG) Neyssa Marina, Children's Oncology Group (COG) **plus** Mark Bernstein, Trial Management Group (Chair)
3.2	Grant holder (UK)	Jeremy Whelan
3.3	Project lead	Matt Sydes
3.4	Clinical Research Scientist	Jane Hook
3.5	Clinical Project Manager	Barbara Uscinska (to Oct-2010) Nicola Kaganson (to Mar-2011) Karen Sanders (- to Sept 2012) Sue Fleck (to April 2013) Nicola Joffe (from April 2013)
3.6	Trial Manager	Sarah Beall (to Oct-2010) Aurélie Faysse (to Dec-2011) Gintare Rutkauskaite (Jan-2012 – April 2013)

[1] See section 8 for others

Area for consideration		Response
3.7	Data Manager	James Pickering
3.8	Statistician (s)	Matt Sydes; Gordana Jovic
4. Trial design		
4.1	Trial flowchart	See Figure 1
4.2	Summary	Osteosarcoma is the most common bone tumour in children and adolescents. The administration of multi-agent chemotherapy has dramatically improved the outcome for these patients. It is known that patients who achieve a good histological response to pre-operative chemotherapy, defined as <10% viable tumour in the resected specimen, experience considerably better survival than those who have a poor response (at least 10% viable tumour). It is not known whether tailoring treatment in order to improve survival in good and poor responders will improve the outcome of these patients. In the absence of promising new agents for this disease, four major osteosarcoma research groups will address this question in a randomised trial. The trial will include all patients with resectable osteosarcoma who would be considered suitable for neo-adjuvant chemotherapy. All patients will receive a standard pre-operative chemotherapy regimen of cisplatin, doxorubicin and methotrexate (MAP). Post operative therapy will be determined by the histological response of the tumour. Good responders will be randomised to continue with MAP, or receive interferon-alpha as maintenance therapy following MAP (MAPifn). Poor responders will be randomised either to continue with MAP or receive the same regimen with the addition of ifosfamide and etoposide (MAPIE). The primary outcome measure is event-free survival.
4.3	Primary outcome measures	• Event free survival
4.4	Secondary outcome measures	• Overall survival • Short-term toxicity • Long-term toxicity • Quality of Life
5. Sample size		
5.1	Sample size summary and rationale	The good histological response rate for the MAP induction regimen is estimated from INT-0133 to be 45%. Analysis of EFS is planned to take place two years after the closure of the trial, analysis of OS is planned for four years after closure. Based on the previous experience of the participating groups, 3-year EFS for the MAP regimen is expected to be 70% for good responders and 45% for poor responders; 5-year OS is also expected to be 70% for good responders and 45% for poor responders. Assuming a two-sided significance level of 5%, 80% power and 400 patients registered per year overall, it was initially proposed that 1260 patients be randomized into EURAMOS-1. Of these, we anticipate 45% good responders (n=567) and 55% poor responders (n=693). Data from COSS suggested that 10% of patients registered at start of treatment are not randomized following surgery. This is for a variety of reasons, including disease progression, insufficient pre-operative chemotherapy and withdrawal of consent. Thus randomization of 1260 patients, accounting for 10% non-randomisation after registration, will require 1400 patients to be registered (630 good responders, 770 poor responders), over a period of 4 years. Randomization of 567 good responders will allow an increase of 10%, from 70% to 80%, to be detected in 3-year EFS and 5-year OS. Randomization of 693 poor responders will allow an increase of

Area for consideration	Response	
	10%, from 45% to 55%, to be detected in 3-year EFS and 5-year OS. The observed non-randomisation rate has been higher (around 30-35%) for many different reasons including disease progression, insufficient preoperative chemotherapy and withdrawal of consent. The trial oversight committees agreed that the trial would require an increased number of patients to be registered to ensure the trial obtains the planned number of events. The protocol was amended in December 2008 to increase the registration sample size to around 2000 patients.	
6. Recruitment		
6.1 Planned start date	1st patient randomised: COSS: 14-Apr-2005 SSG: 20-Apr-2005 EOI: 19-Sep-2005 COG: 06-Dec-2005	
6.2 Planned completion date	The trial closed to registrations on 30 June 2011 with 2260 patients registered. Randomisation was completed on 7 November 2011 with 1332 patients randomised. The trial will end on the date of the last treatment visit for the last patient undergoing protocol treatment. Long term follow-up will continue for a minimum of five years after the end of the trial.	
7. Protocol		
7.1 Protocol signed off?	Yes	
8. Trial team		
8.1 Trial team status	X	Trial Management Group
		Trial Development Group
8.2 Other TMG / TDG members	**Name**	**Role**
	Mark Bernstein	Chair
	Neyssa Marina	COG Chief Investigator
	Mark Krailo	COG Statistician
	Possi Gontijo	COG Protocol Coordinator
	Stefan Bielack	COSS Chief Investigator
	Joachim Gerss	COSS Statistician
	Matthias Kevric	COSS Data Manager
	Jeremy Whelan	EOI Chief Investigator
	Matt Sydes	Project Lead & Trial Statistician
	Jane Hook	Clinical Research Scientist
	Gordana Jovic	Statistician
	Karen Sanders	Clinical Project Manager
	Sue Fleck	Clinical Project Manager
	Nicola Joffe	Clinical Project Manager
	Gintare Rutkauskaite	Trial Manager
	James Pickering	Data Manager
	Sigbjørn Smeland	SSG Chief Investigator
	Elisabeth Johanson	SSG Statistician
	Eva-Mari Olofsson	SSG Data Manager
8.3 TMG charter signed off?	Yes	

Area for consideration	Response	
9. International collaborations		
9.1 Collaborative groups	**Name**	**Role**
	Children's Oncology Group (COG), Canada	Data centre for USA, Canada, Australasia
	German-Austrian-Swiss Cooperative Osteosarcoma Study Group (COSS), Germany	Data centre for Austria, Germany, Hungary, Switzerland, Czech Republic
	European Osteosarcoma Intergroup (EOI), UK	Data centre for Belgium, Ireland, Netherlands, United Kingdom.
	Scandinavian Sarcoma group (SSG), Sweden	Data centre for Denmark, Finland, Norway, Sweden
	EURAMOS Intergroup Safety Desk (EISD), Germany	Safety Desk for EURAMOS-1 trial.
	Quality of Life Co-ordinating Center (QLCC), Germany	Coordinates Quality of Life study
	Coordinating Center for Quality Matters (CCQM), Germany	Quality Assurance & consistency in trial conduct
9.2 Industry partners	**Name**	**Role**
	Merck & Co. (formerly Schering Plough)	Provide Peg-Intron free of charge for patients randomised to MAPifn treatment
9.3 Sub-contractors	**Name**	**Role**
	None	
10. Independent Data Monitoring Committee		
10.1 Membership Chair	Barry Hancock, Sheffield, UK	
Member:	Gerald Gilchrist, Minnesota, USA	
Member:	Otilia Dalesio, Amsterdam, NL	
Member:	Peter Hoglund, Lund, Sweden	
10.2 IDMC Charter signed off?	Yes	
11. Trial Steering Committee		
11.1 Membership Chair:	Stefano Ferrari, Bologna, Italy	
Member:	Joe Mirro, Memphis, USA	
Member:	Hans Strander, Stockhom, Sweden	
Member:	Robert Souhami, London, UK	
Member:	Stefan Bielack, Stuttgart, Germany	
Member:	Mark Bernstein, Halifax, Canada	
Member:	Neyssa Marina, Stanford, USA	
Member:	Sigbjørn Smeland, Oslo, Norway	
Member:	Jeremy Whelan, London, UK	
Member:	Representative from the Coordinating Data Centre	
11.2 TSC Charter signed off?	Yes	
12. Trial Status		
12.1 Status		In design
		Accrual continues
	X	Accrual closed, follow-up ongoing, main results unknown
		Accrual closed, follow-up ongoing, main results known

Area for consideration	Response
13. Recruitment	
13.1 Date of first pt randomised	COSS: 14-Apr-2005 SSG: 20-Apr-2005 EOI: 19-Sep-2005 COG: 06-Dec-2005
13.2 Time since trial opened (m)	75 months since accrual started (to 30-Jun-2011) Activation date: 15 December 2004
13.3 Target recruitment by now	Recruitment completed
13.4 Actual recruitment now	Observed registrations: 2260 (complete) Observed randomisations: 1332 (complete)
13.5 Date accrual stopped	30 June 2011
13.6 Graph of recruitment	See Figure 2 to 5
13.7 Recruitment by group/country	See Table 1
13.8 Recruitment issues & problems	The rate of non-randomisation after registration was much higher than anticipated, at approximately 35% rather than 10%. See Figures B2, B3 and B4. There are many reported reasons. Consequently, in 2008, accrual was extended to around 2000 patients. The trial closed to registrations on 30 June 2011 with 2260 patients registered. .The extra accrual should lead to maturity of the poor response comparison as soon as possible. The results of the good response comparison is to be presented at ASCO in June 2013.
13.9 Acceptance rate	Acceptance rate not collected at Coordinating Data Centre
14. Organisational problems	
14.1 Organisational problems	None this year
15. Issues specific to the trial, including substudies	
15.1 Issues for main trial	The triggers for the main analysis of event-free survival in the Good Response randomisation was reached (more than 147 events reported). Date was frozen for this analysis on 15th Feb 2013 and results will be presented at the ASCO annual meeting on 3rd of June.
15.2 Issues for sub-studies	**Quality of Life**: The Quality of Life study is being co-ordinated by the Quality of Life panel and the Coordinating Data Center for Quality of Life. Initial data collection is good but there are problems in gaining forms for the later assessments. Baseline data were presented at ASCO 2010 and preliminary results of the initial treatment period were presented at SIOP 2011. **Biological Studies:** Samples in North America are being collected as part of a separate osteosarcoma biology study. Studies include array analysis as well as studies of specific genes that may lead to drug resistance or that are oncogenes aiding in the development of the malignant phenotype, or tumour suppressor genes silenced during oncogenesis. In Europe, expression analyses and genomic arrays are ongoing. The TMG are taking ongoing active steps to ensure trans-Atlantic cooperation between the North American and European biological and pathological experts. A meeting was held in Stuttgart to move this forward. A charter has subsequently been drafted but has not been finalised due to problems raised by one pathologist. Biological studies have been discussed at several TMG meetings in 2011. There remain difficulties in coordinating the studies. This It was agreed at the Jun-2013 TMG meeting that this will be raised again at the next TMG meeting.

Area for consideration	Response
16. Data completeness	
16.1 Completeness of data collected	Data return rates for randomised patients are presented in Table 2. Data return has generally been good. There have been problems accessing (non-)randomisation forms for COG patients that were not randomised, but reasons for non-randomisations have been supplied this year and are under review. Data cleaning for Good Response analysis is ongoing.
16.2 Adherence to schedules	The treatment schedules are mostly well followed but there are some notable deviations. For example, according to the Sep-12 data transfer, there are 3 randomised patients who appear to have received >2 cycles of doxorubicin and 4 who received >2 doses of cisplatin; this should make these patients ineligible for randomisation. These deviations may be due to coding errors or may be real. The CDC have investigated to resolve this.
16.3 Problem centres	Each Data Centre corresponds directly with the sites. The CDC does not have information available by site. There are no reported problem sites.
17. Changes to trial since last Annual Report	
17.1 Protocol modifications	Version 3.0, 21-Jul-2011 Version 2.1, 21-Apr-2009 Version 2.0, 31-Dec-2008 (Version 2 onwards reflects the changes in planned sample size) Version 1.3, 31-Jul-2007 Version 1.2, 30-Mar-2007 Version 1.1, 30-Jun-2006 Version 1.0, 30-Sep-2004
17.2 Current protocol version	Version 3.0, 21 July 2011 Appendix A Version 3.0, 21 July 2011 Appendix B Version 4.0, 21 July 2011
17.3 Sample size modifications?	The change in sample size to a target of *around* 2000 patients registered was agreed and made in protocol amendment Version 2.0, 31-Dec-2008. The decision to extend recruitment into 2011 did not necessitate a protocol-amendment as the sample size remained *around* 2000 patients. However, an amendment to the COG group-specific appendix was made to state that enrolment would be "extended to 30 June 2011 to obtain the maximum enrolment of 2300". For EOI, COSS and SSG no amendment was required.
17.4 Changes in TMG membership?	At EOI/CDC, Gintare Rutkauskaite has left as Trial Manager (not formally replaced, yet) and Nicola Joffe (nee Kaganson) has replaced as CPM Sue Fleck who had taken over from Karen Sanders.
17.5 Changes in DMC membership?	No changes since the last IDMC meeting
17.6 Sub-studies activated?	N/A
17.7 External requests for data?	Newcastle (EOI group site) has requested to be allowed to include outcome data from their patients enrolled in EURAMOS-1 in a local study looking at candidate genes in osteosarcoma. Investigators for the SPECS (evaluating cancer signatures) and TARGET (uncovering genomic factors distinguishing groups of children with favourable prognosis and those that do not respond to treatment) studies have requested access to outcome data by the end of this calendar year at the earliest. Even though it would be known that patients came from sarcoma studies, EURAMOS-1 would only be a proportion (<50%).

Area for consideration	Response		
18. Competing trials			
	Trial ID	**Relevance**	**More info**
18.1 Directly competing trials	NCT00470223	Same patients	FNCLCC is recruiting patients to a trial of zoledronic acid (n=440)
	NCT00667342	Same patients	St Jude's has a study of bevacizumab (n=95). Clinicaltrials.gov is unclear on this study: it is listed as phase III but has only one arm
	NCT00691236	High Grade OS	Tata Memorial Hospital, India. is recruiting patients to a 3-arm trial of zoledronic acid (n=60)
18.2 Relevant forthcoming trials	**None**		
18.3 Other relevant information	Mifamurtide (MTP) gained a marketing authorisation in Europe in March 2009. MTP is becoming increasingly available in Europe but has not been approved by the FDA for use in North America. MTP did not have a direct impact on accrual in EURAMOS-1.		
19. Independent Data Monitoring Committee			
19.1 IDMC meeting history	**Date**	**Format**	
	28 November 2012	In person	
	21 November 2011	In person	
	2 December 2010	In person / via WebEx	
	3 November 2009	In person	
	9 December 2008	In person	
	22 October 2007	In person	
	16 May 2007	In person	
	24 October 2006	In person	
	05 May 2006	In person	
20. Trial Management Group			
20.1 TMG meeting history	**Date**	**Format**	
	03-Jun-2013	In person (mini-TMG meeting)	
	xx-Mar-2013	Teleconference (expanded)	
	23 Jan 2013	Teleconference	
	05 Sep 2012	Teleconference	
	18 Apr 2012	Teleconference	
	20 Oct 2011	Teleconference	
	20 Aug 2011	Teleconference	
	16 May 2011	Teleconference	
	23 Feb 2011	Teleconference	
	13 Oct 2010	Teleconference	
	22 Apr 2010	Teleconference	
	25 Jan 2010	Teleconference	
	16 Sep 2009	Teleconference	
	22 Oct 2008	In person	

Area for consideration	Response	
	10 Sep 2008	Teleconference
	12 Jun 2008	Teleconference
	25 Jan 2008	In person
	21 Jun 2007	Teleconference
	05 Mar 2007	Teleconference
	10 Mar 2006	Teleconference
	16 Jan 2006	Teleconference
	31 Oct 2005	In person/Teleconference
	14 Jun 2005	In person
	14 Dec 2004	Teleconference
	15 Sep 2004	In person
	04 Jun 2003	In person
	29 Jan 2003	In person

21. Publication, presentation and dissemination

	Date	Published Reference / Conference
21.1 Published papers	Mar 2011	Heidi Oellers. Monitoring 'Investigator initiated trials' (ITTs(=) Oder: So viel wie notig. So wenig wie moglich. Mitteilungen der Deutschen *Geselischaft fur Gute Forschungspraxis e.V.,* issue 58, März 2011, page 9 - 10
	2010	Marina N, Bielack S, Whelan J, Smeland S, Krailo M, Sydes S et al. International Collaboration is Feasible in Trials for Rare Conditions: The EURAMOS Experience. *Cancer Treat Res* 152:339-353, 2010.
21.2 Abstracts	May 2012	Jeremy Whelan, Jane Hook, Stefan S. Bielack, Neyssa Marina, Sigbjorn Smeland, Gordana Jovic, Mark D. Krailo, Thomas Kühne, Mikael Eriksson, Trude Butterfass-Bahloul, Lisa A. Teot, Leo Kager, Hans Gelderblom, Kirsten Sundby Hall, Pancras C. W. Hogendoorn, Matthew Robert Sydes, Mark L. Bernstein and EURAMOS. EURAMOS-1 study: Recruitment, characteristics, and initial treatment of more than 2,000 patients (pts) with high-grade osteosarcoma. Journal of Clinical Oncology, 2012 ASCO Annual Meeting Proceedings (Post-Meeting Edition). Vol 30, No 15_suppl (May 20 Supplement), 2012: 10081© 2012 American Society of Clinical Oncology
	Mar 2012	Jane Hook, Leonardo Trani, Gordana Jovic, Aurélie Faysse, James Pickering, Karen Sanders, Mark Bernstein, Stefan Bielack, Neyssa Marina, Sigbjorn Smeland, Matthew R. Sydes, Jeremy Whelan on behalf of the EURAMOS-1 Investigators. EURAMOS-1 (NCT00134030), a collaborative international randomised phase III trial in osteosarcoma: the UK experience. British Sarcoma Group Conference 2012.
	Oct 2011	Zils K, Marina N, Bielack S, Jovic G, Pickering J, Sydes M, Smeland S, Whelan J, Bernstein M. Lack of centralization and under-rectruiting of young-adults: lessons from EURAMOS-1/AOST0331 (NCT00134030). Abstract for SIOP 2011 in Auckland (October 2011)
	Oct 2011	Wiener A, Nagarajan R, Hjorth L, Jenney M, Bernstein M, Krailo M, Sydes M, Calaminus G. Quality of life (QoL) in osteosarcoma: preliminary results of the initial treatment period of EURAMOS-1 (NCT00134030),

Area for consideration	Response	
		Abstract for SIOP 2011 in Auckland (October 2011)
	May 2010	Wiener A, Nagarajan R, Hjorth L, Jenney M, De Vos P, Bernstein ML et al. Quality of life (QoL) in osteosarcoma: First results of the presurgery treatment period of EURAMOS-1 (NCT00134030). J Clin Oncol 28:Abstr 10062, 2010.
	May 2010	Stefan Bielack, Gordana Jovic, Neyssa Marina; Sigbjørn Smeland, Matthew R. Sydes, Jeremy Whelan, Mark Bernstein. Age-specific recruitment variations in a large intergroup osteosarcoma study, EURAMOS-1 (NCT00134030) (to be published in J Bone Joint Surg Br 2011)
	May 2009	S. Smeland, S. Bielack, M. Sydes, T. Butterfass-Bahloul, G. Calaminus, N. Marina, M. Tomiczek, J. Whelan, and M. Bernstein. The European and American osteosarcoma study group protocol, EURAMOS-1: successful transatlantic cooperation in osteosarcoma. J Bone Joint Surg Br 2010 92-B: 438
	Nov 2008	Carrle D, Kühne T, Zoubek A, Bielack S. EURAMOS1/COSS – Progress report. Monatsschr Kinderheilkd 2008; 156: 1035. Vienna, Austria
	May 2008	Bielack S, Sydes M, Butterfass-Bahloul T, Calaminus G, Carrle D, Marina N et al. 2008 Update On The European And American Osteosarcoma Study EURAMOS1 (A Trial Conducted As Part Of ECT-EUROCORES). Ortopedia Traumatologia Rehabilitacja 10 [EMSOS 2008 Supplement], 20-Abstract O10. 2008.
	Feb 2008	Whelan J, Sydes M, Bielack S, Smeland S, Marina N, May B et al. Successful trans-Atlantic collaboration in a randomised controlled trial in osteosarcoma:EURAMOS1 (ISRCTN67613327; a trial conducted as part of ECT EUROCORES) - a potential model for collaboration in rare diseases. British Sarcoma Group meeting 2008 conference abstracts http://www.bsgconference.org.uk/abst2008/absp-sydes.pdf. 2008.
	Oct 2007	Whelan J, Smeland S, Marina N, Bernstein M, Sydes MR, May EE et al. Successful trans-Atlantic collaboration in a randomised controlled trial in osteosarcoma: EURAMOS1 (ISRCTN67613327; a trial conducted as part of ECT-EUROCORES) - a potential model for collaboration in rare diseases. Proceedings of the National Cancer Research Institute Conference 2007, 60 (A171). 2007.
	Jun 2007	Marina N, Bielack S, Sydes M, Bernstein M, Butterfass-Bahloul T, Smeland S et al. International collaboration is feasible in trials for rare conditions: the EURAMOS experience. Journal of Clinical Oncology, 2007 ASCO Annual Meeting Proceedings Part I. **25**[18S], Abstract 20501. 20-6-2007.
	2007	Whelan J, Smeland S, Marina N, Bernstein M, Sydes M, May B et al. Successful pan-European and trans-Atlantic collaboration in a randomised controlled trial in osteosarcoma: EURAMOS1 (ISRCTN67613327; a trial conducted as part of ECTEUROCORES). European Journal of Cancer Supplements 5[4], 408-409. 2007.
	Jun 2007	**Sarcoma, vol. 2007, Article ID 76405** Pan-European Sarcoma Trials: Moving Forward in a Climate of Increasing Economic and Regulatory Pressure

21.3 Presentations / promotions Poster	Jul 2012	**ASCO 2012** EURAMOS-1 study: Recruitment, characteristics, and initial treatment of more than 2,000 patients (pts) with high-grade osteosarcoma.Jeremy Whelan, Jane Hook, Stefan S. Bielack, Neyssa Marina, Sigbjorn Smeland, Gordana Jovic, Mark D. Krailo, Thomas Kühne, Mikael Eriksson, Trude Butterfass-Bahloul, Lisa A. Teot, Leo Kager, Hans Gelderblom, Kirsten Sundby Hall, Pancras C. W. Hogendoorn, Matthew R. Sydes, Mark L. Bernstein on behalf of the EURAMOS investigators**.**
Oral	May 2012	**EMSOS 2012** Institutional variables in the European and American Osteosarcoma Study EURAMOS-1: Pediatric and adolescent vs. young adult osteosarcoma patients. Stefan Bielack, Jane Hook, Gordana Jovic, Neyssa Marina; Sigbjørn Smeland, Matthew R Sydes, Jeremy Whelan, Mark Bernstein
Workshop	Feb 2012	**2nd International Meeting on Future Clinical Trials for the Adjuvant Treatment of Osteosarcoma: Creating a Strategic Consensus**. Chaired by Jeremy Whelan. London, UK
Oral	May 2011	**EMSOS 2011** Osteosarcoma treatment in Europe and elsewhere is far from being centralized: Lessons from EURAMOS-1 (NCT00134030). Stefan Bielack
Workshop	Mar 2010	**1st International Meeting on Future Clinical Trials for the Adjuvant Treatment of Osteosarcoma: Prioritising the Questions.** Chaired by Jeremy Whelan. London, UK
Oral	Nov 2009	**Connective Tissue Oncology Society Meeting** EURAMOS1/COSS – A successful transatlantic co-operation in Osteosarcoma. Dorothe Carrle
Oral	Jul 2009	**EFGCP Meeting** Interaction with competent authorities in a pan-European investigator-driven trial: the EURAMOS-1 experience. Matthew Sydes
Oral	Nov 2008	**German Paediatric Oncology Fall Meeting.** EURAMOS1/COSS – Progress report. Vienna, Austria
Workshop	Oct 2008	**COG Fall Meeting. EURAMOS-1 Investigators meeting.** Denver, USA**.**
Workshop	Sep 2008	**EU-Directive 2001/20/EC:** In his function as project leader of the ESF/ECT-EURAMOS, Stefan Bielack participated in the scientific organising committee of an ESF Forward Look activity on Clinical trials and co-chaired 1 of the 5 strategic themes, namely "Management of Investigator Driven Clinical Trials". A strategic workshop on this theme was held in London on 29.05.08 and its results were further discussed and refined at the Consensus Conference Investigator-Driven Clinical Trials held in Strasbourg on 29-30.09.08, which resulted in key recommendations on future strategies to strengthen investigator driven clinical trials and patient oriented research in Europe.
Oral	May 2008	**EMSOS 2008** Update on the European and American Osteosarcoma Study EURAMOS1 (a TRIAL CONDUCTED AS PART OF ECT-EUROCORES). Warsaw, Poland.
Poster	Feb 2008	**BSG 2008.** Successful trans-Atlantic collaboration in a randomised controlled trial in osteosarcoma: EURAMOS-

		1 – a potential model for collaboration in rare diseases. Sheffield, UK.
Workshop	Jan 2008	**Pan European Clinical Trials under current EU Regulations,** A training course for data managers, study nurses and junior clinical investigators initiated by the EURAMOS group, COSS, KKS Muenster, EOI and SSG. London, UK.
Poster	Oct 2007	**NCRI Cancer Conference 2007** Feasibility and accrual. Birmingham, UK
Poster	Sep 2007	**ECCO 14** Feasibility and accrual. Barcelona, Spain
Oral	May 2007	**EMSOS 2007** An update of EURAMOS 1. Porto, Portugal
Oral	May 2007	**American Society of Pediatric Hematology-Oncology:** EURAMOS1, presented in an osteosarcoma symposium. Toronto, Canada
Oral	Nov 2006	**CTOS, 2006** EURAMOS update. Venice, Italy.
Workshop	Oct 2006	**Pan European Clinical Trials under current EU Regulations,** A training course for data managers, study nurses and junior clinical investigators initiated by the EURAMOS group, COSS, KKS Muenster, EOI and SSG. Oslo, Norway.
Workshop	Dec 2005	**Pan European Clinical Trials under current EU Regulations** A training course for data managers, study nurses and junior clinical investigators initiated by the EURAMOS group, COSS, KKS Muenster, EOI and SSG. Stuttgart, Germany.
Oral	Oct 2005	**ECCO 2005** • A multinational, transatlantic study in "classical" osteosarcoma patients - European and Americal Osteosarcoma Study EURAMOS-1. Paris, France. • How can we perform multinational trials without breaking the law? • How can coordinating data centres function in pan-European trials? Obligations & Infrastructure, as exemplified by EURAMOS 1 • Who pays? Funders perspective, by the European Science Foundation
Oral	Autumn 2005	**GPOH 2005** Durchführung von Therapiestudien unter 12. AMG-Novelle und GCP am Beispiel der EURAMOS 1 Studie der COSS-Gruppe
Oral	2005	**EMSOS 2005** The European Science Foundation's Pan-European Clinical Trials (ECT) EUROCORES: EURAMOS 1: Scientific, regulatory and funding issues of a Pan-European / American osteosarcoma study. Trieste, Italy.
Oral	June 2005	**SMS 2005** EURAMOS 1: A model for the future of clinical research in osteosarcoma. Stuttgart, Germany.
Oral	2005	**Jahrestagung der Arbeitsgemeinschaft Knochentumoren** EURAMOS: Die neue europäisch-amerikanische Osteosarkomstudie

Figure 1: Trial Design

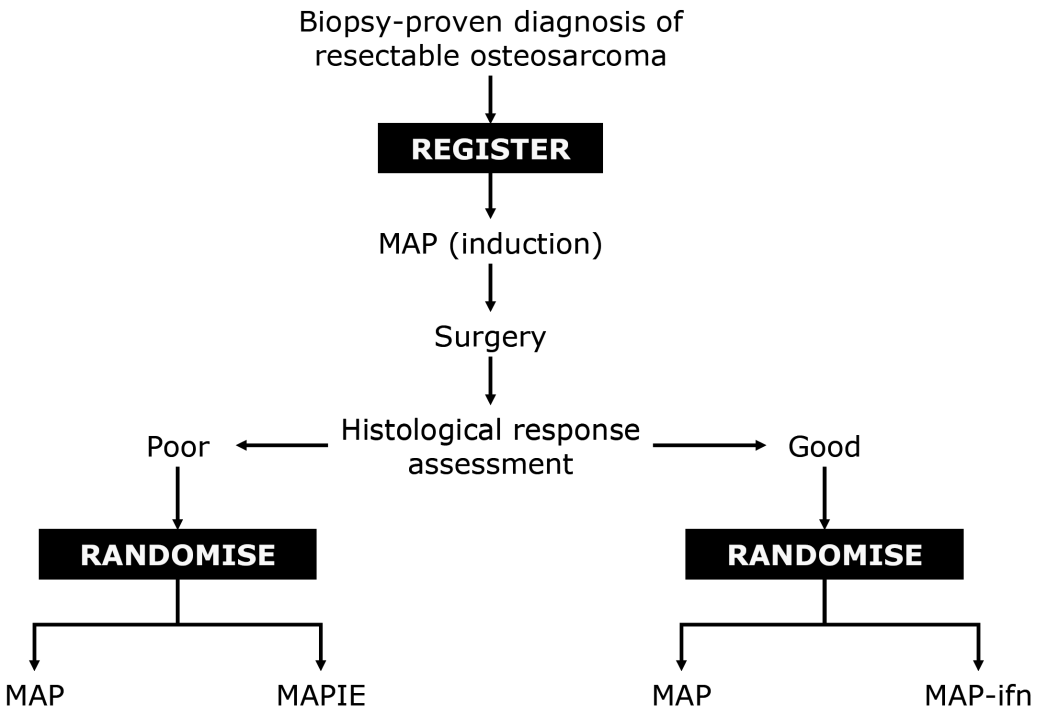

Figure 2: Cumulative expected & observed registrations (to 30-Jun-2011)

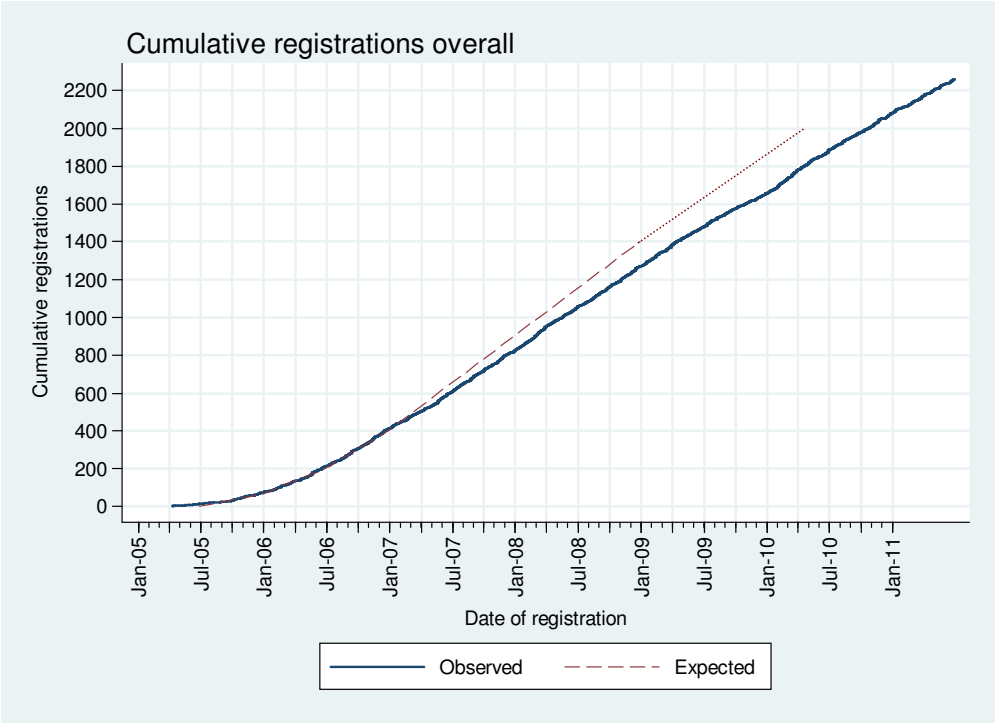

Figure 3: Cumulative observed randomisations (to end Nov-2011)

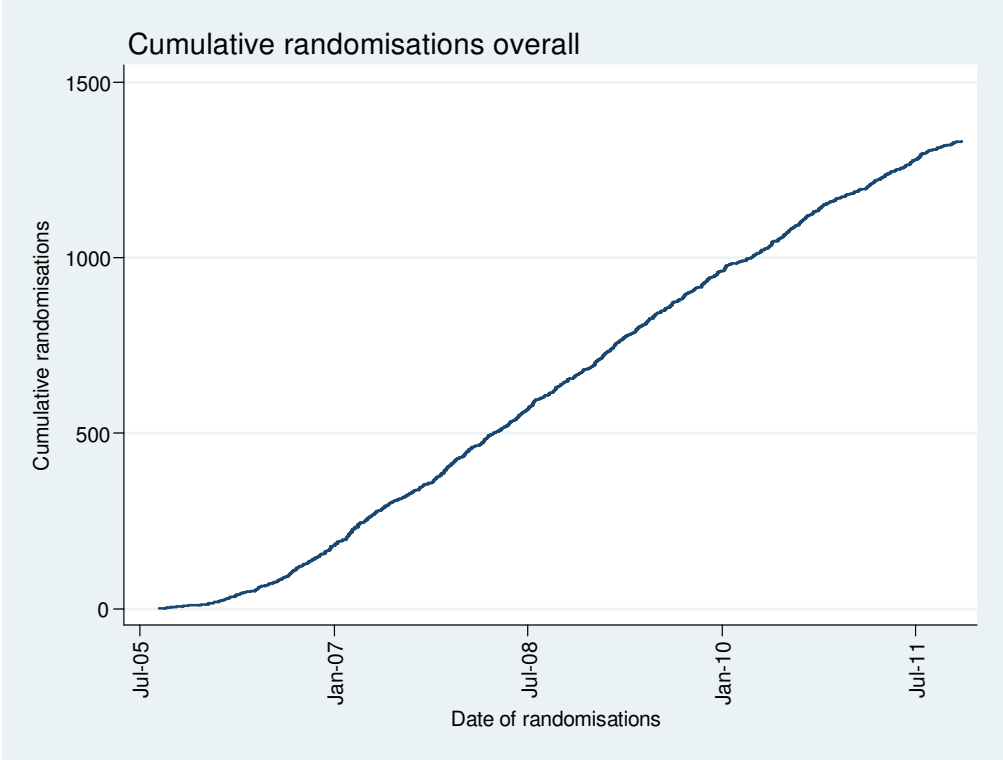

Figure 4: Cumulative expected and observed randomisations in good responders (to end Nov-2011)

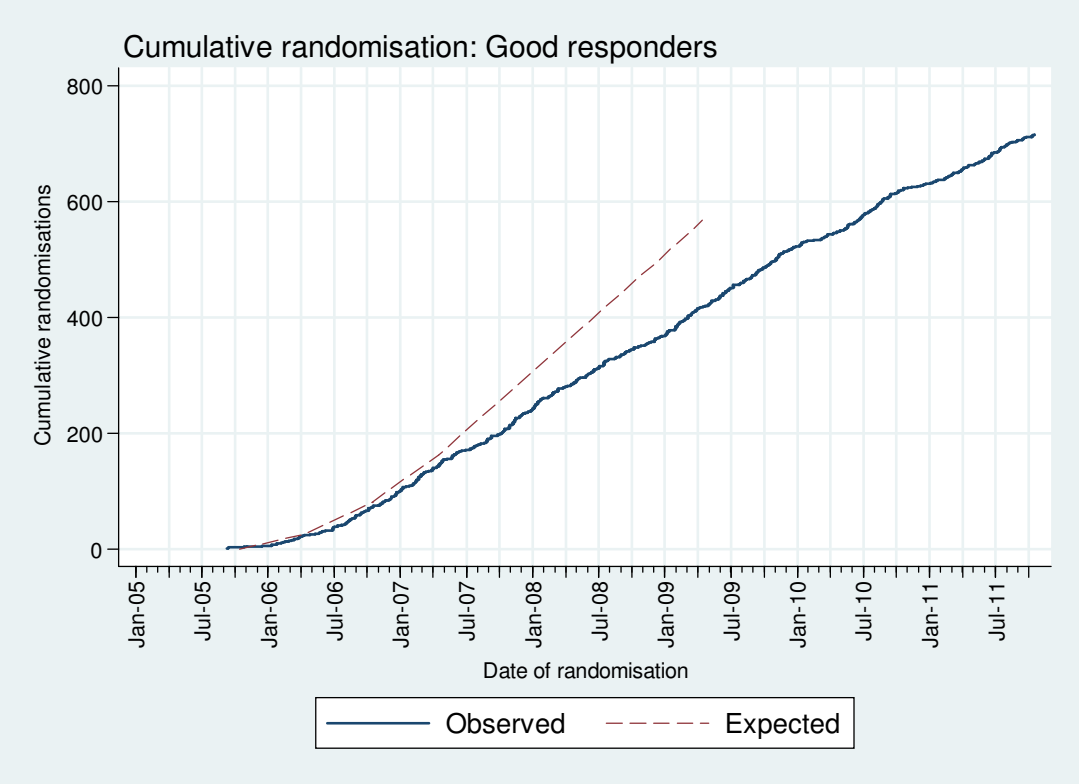

Figure 5: Cumulative expected and observed randomisations in poor responders (to end Nov-2011)

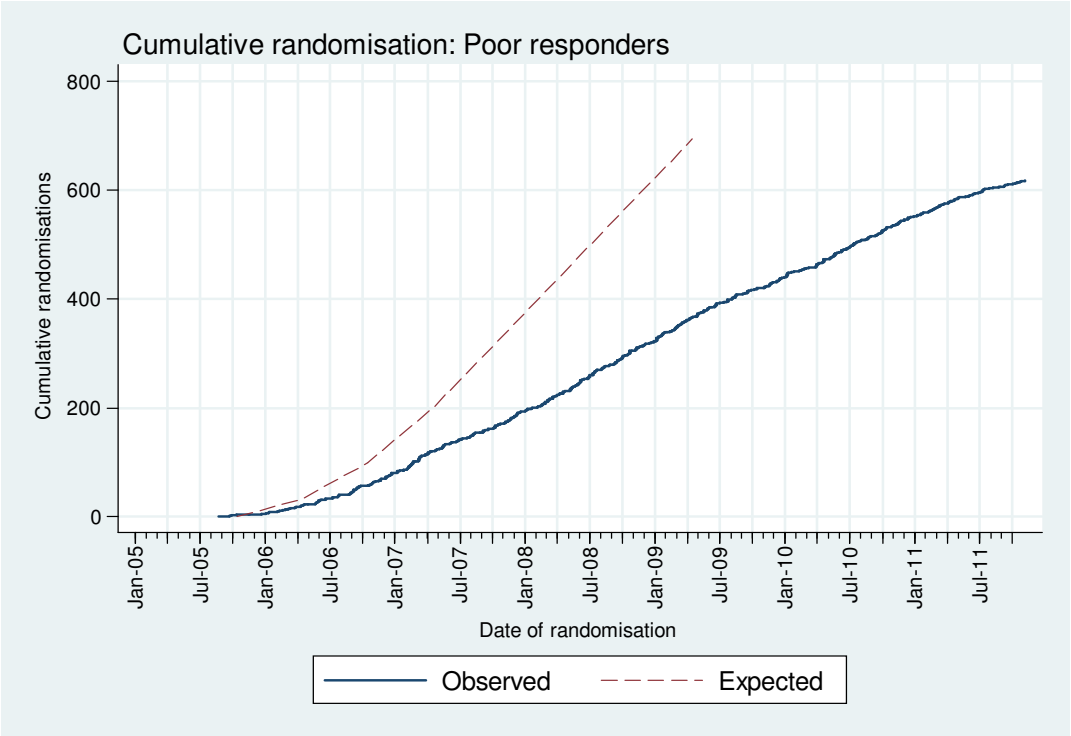

Table 1: Recruitment by Group/Country (to end Nov-2011)

COG	Nb sites	Registrations	Randomisations
Australia	6	28	13
Bahamas	2	2	0
Canada	15	82	46
Guatemala	1	1	1
New Zealand	3	14	5
Puerto Rico	1	5	1
Switzerland	3	12	5
USA	152	1020	540
TOTAL	**183**	**1164**	**611**

COSS	Nb sites	Registrations	Randomisations
Austria	5	28	20
Czech Rep.	2	9	6
Germany	85	432	298
Hungary	2	24	19
Switzerland	5	27	20
TOTAL	**99**	**520**	**363**

EOI	Nb sites	Registrations	Randomisations
Belgium	6	52	44
Ireland	1	6	1
Netherlands	4	101	65
UK	24	298	166
TOTAL	**35**	**457**	**276**

SSG	Nb sites	Registrations	Randomisations
Denmark	2	27	12
Finland	1	3	3
Norway	3	41	34
Sweden	6	48	33
TOTAL	**12**	**119**	**82**

Table 2: Data Return rates for randomised patients (to 15-Sep-2011)

All groups	Forms expected		Received but not yet expected	Total received
Form	**Received**	**Overdue**		
Registration	1312 (100%)	0 (0%)	0	**1312**
Biopsy	1255 (96%)	51 (4%)	4	**1259**
Pre-operative chemotherapy	1304 (99%)	8 (1%)	0	**1304**
Surgery	1302 (99%)	10 (1%)	0	**1302**
Resected specimen	1265 (97%)	41 (3%)	4	**1269**
Randomisation	1306 (100%)	0 (0%)	6	**1312**
Post-operative chemotherapy	1129 (92%)	99 (8%)	10	**1139**
End of treatment	1107 (90%)	122 (10%)	6	**1113**
Interferon 12 month form	291 (94%)	18(6%)	2	**293**
Interferon 15 month form	156 (88%)	22 (12%)	2	**158**
Interferon 18 month form	134 (88%)	19 (13%)	3	**137**
Interferon 21 month form	120 (87%)	18 (13%)	2	**122**
Interferon 24 month form	100 (75%)	32 (24%)	1	**101**
All forms	**10781 (96%)**	**440 (4%)**	**40**	**10821**