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A randomised trial of the EURopean and AMerican Osteosarcoma Study group to optimize treatment strategies for resectable osteosarcoma based on histological response to pre-operative chemotherapy

Submission date 24/08/2004	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 30/09/2004	**Overall study status** Completed	
Last Edited 19/10/2018	**Condition category** Cancer	

Plain English summary of protocol
http://www.cancerhelp.org.uk/trials/a-trial-looking-at-treatment-after-surgery-for-people-with-osteosarcoma

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2004-000242-20

ClinicalTrials.gov (NCT)

NCT00134030

Protocol serial number
N/A

Study information

Scientific Title
A randomised trial of the EURopean and AMerican Osteosarcoma Study group to optimize treatment strategies for resectable osteosarcoma based on histological response to pre-operative chemotherapy

Acronym
EURAMOS 1

Study objectives
Study hypothesis added as of 10/09/2008:

Primary objectives:
1. To examine, in a randomised controlled trial, whether the addition of ifosfamide and etoposide (IE) to post-operative chemotherapy with cisplatin, doxorubicin and methotrexate improves event-free survival for patients with resectable osteosarcoma and a poor histological response to 10 weeks of pre-operative chemotherapy.
2. To examine, in a randomised controlled trial, whether the addition of interferon-alpha ifn) as maintenance therapy after post-operative chemotherapy with cisplatin, doxorubicin and methotrexate improves event-free survival for patients with resectable osteosarcoma and a good histological response to 10 weeks of pre-operative chemotherapy.

Secondary objectives:
3. To investigate whether the addition of IE to post-operative therapy for poor responders, and the addition of ifn as maintenance therapy for good responders, leads to an improvement in overall survival, short-term toxicity, long-term toxicity and quality of life.
4. To investigate whether the addition of IE to post-operative therapy for poor responders, and the addition of ifn as maintenance therapy for good responders, leads to an improvement in event-free and overall survival in patients with localized osteosarcoma at entry.
5. To investigate whether biological or clinical correlates to histological response and outcome can be identified.
6. To establish whether this international cooperation in clinical trials for osteosarcoma is feasible.

Please note that the target number of participants has been added as of 10/09/2008.

On 08/02/2011 the overall trial end date was changed from 30/03/2009 to 30/06/2011.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Trent Multi-centre Research Ethics Committee, 07/01/2005, ref: 04/MRE04/79

Study design

Randomised controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Osteosarcoma

Interventions
All patients who are registered on this study will receive pre-operative chemotherapy with MAP for about 10 weeks. Following surgery for the primary tumour, the histological response to pre-operative chemotherapy will be assessed. Good responders (<10% viable tumor) will be randomized to receive either MAP or MAPifn. Poor responders (≥10% viable tumor) will be randomized to receive either MAP or MAPIE.
MAP = methotrexate, doxorubicin and cisplatin
MAPifn = methotrexate, doxorubicin and cisplatin followed by pegylated interferon alpha
MAPIE = methotrexate, doxorubicin, cisplatin, ifosfamide and etoposide

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Methotrexate, doxorubicin, cisplatin, pegylated interferon alpha, ifosfamide, etoposide

Primary outcome(s)
Added as of 10/09/2008:
Event-free survival

Key secondary outcome(s))
Added as of 10/09/2008:
1. Overall survival
2. Toxicity as measured by CTCAE v3.0
3. Quality of life

Completion date
30/06/2011

Eligibility

Key inclusion criteria
Eligible patients will be registered, then following assessment of histological response of primary tumor, may be eligible for randomisation.

Patients must fulfill the following criteria for registration into the trial:
1. Histological evidence of high grade osteosarcoma of the extremity or axial skeleton including those arising as second malignancies
2. Resectable disease
3. Aged 40 years or less at date of diagnostic biopsy
4. Registration within 30 days of diagnostic biopsy
5. Start chemotherapy within 30 days of diagnostic biopsy
6. Neutrophils more than or equal to 1.5 x 10^9/L (or white blood cell count [WBC] more than or equal to 3 x 10^9/L if neutrophils are not available) and platelet count more than or equal to 100 x 10^9/L
7. Glomerular Filtration Rate more than or equal to 70 ml/min/1.73 m^2
8. Serum bilirubin more than or equal to 1.5 x Upper Limit of Normal [ULN]
9. Sufficient cardiac function to receive anthracyclines: shortening fraction (SF) more than or equal to 28% or ejection fraction (EF) more than or equal to 50%
10. Adequate performance status (Karnofsky score more than or equal to 60 or World Health Organisation [WHO] less than or equal to two for patients [aged 16 or over], Lansky score more than or equal to 60 [aged under 16]). Patients whose performance status is adversely affected by a pathologic fracture but who are able to undergo treatment are eligible.
11. Patient fit to undergo protocol treatment and follow-up
12. Written informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Sex
All

Key exclusion criteria
1. Unresectable disease, primary or metastatic or both
2. Low grade osteosarcoma
3. Juxtacortical (periosteal, parosteal) osteosarcoma
4. Craniofacial osteosarcoma
5. Any previous treatment for osteosarcoma
6. Any previous chemotherapy for any disease
7. Any other medical condition precluding treatment with protocol chemotherapy (for example Human Immunodeficiency Virus [HIV], psychiatric disorder etc.)
8. Pregnant or lactating women

Patients must fulfill the following criteria for randomisation into the trial:
1. Assessment of histological response in primary tumor within 35 days of definitive surgery
2. Exactly two courses of cisplatin and doxorubicin must have been administered before surgery
3. At least two courses and no more than six courses of methotrexate must have been administered before surgery
4. Recovery from prior therapy allowing administration of chemotherapy

5. No progression of metastatic disease or new metastatic disease
6. Macroscopically complete surgical resection of the primary tumor
7. In patients with metastatic disease, complete removal of all metastases or complete removal planned and deemed feasible
8. Age more than or equal to five for patients with good response
9. Essential data collection will be provided
10. Written consent to undergo randomisation

Date of first enrolment
30/03/2004

Date of final enrolment
30/06/2011

Locations

Countries of recruitment
United Kingdom

England

Austria

Belgium

Canada

Czech Republic

Finland

Ireland

New Zealand

Puerto Rico

Switzerland

United States of America

Study participating centre
The Middlesex Hospital
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Sponsor information

Organisation
Medical Research Council (UK)

ROR
https://ror.org/03x94j517

Funder(s)

Funder type
Research organisation

Funder Name
European Science Foundation (ESF)

Alternative Name(s)
The European Science Foundation (ESF), ESF - European Science Foundation, ESF

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
France

Funder Name
Clinical Trials Awards and Advisory Committee (UK)

Funder Name
Deutsche Krebshilfe (Germany)

Funder Name
Swedish Cancer Society and Nordic Cancer Union (Scandinavian countries)

Funder Name

Childrens Oncology Group (USA)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/02/2015		Yes	No
Results article	results	10/07/2015		Yes	No
Plain English results				No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes