Response from Dr J Whelan, co chair EURAMOS Strategy Group, chair National Cancer Research Institute Bone sarcoma subgroup

i. The EURAMOS Strategy Group includes representatives of all major international and national osteosarcoma study groups conducting clinical trials in this desease. Its goals include
   a. development of a programme of clinical research to improve survival from osteosarcoma
   b. conceive new studies
   c. oversee study development with consideration to value, scientific validity, feasibility
   d. be responsible for core strategic policy of EURAMOS group
   e. develop relationships with partners including investigators, funders, regulatory bodies, industry

ii. EURAMOS-1, the first clinical trial of this coalition, completed accrual in June 2011, having included over 2,100 patients since opening in March 2005.

iii. In March 2010, an international consensus meeting was held to consider the most important questions to be addressed in future randomised trials of adjuvant chemotherapy for resectable osteosarcoma. There was unanimous agreement that a further trial of mifarmurtide should be conducted to provide more robust evidence for any effect of mifarmurtide added to standard chemotherapy and for this to be associated with appropriate translational studies to identify a mechanism of action and potential sub groups who may benefit to a greater or lesser extent from this agent.

iv. Discussions took place with Takeda to undertake this study which it was estimated could be completed within five years. In December 2010, Takeda withdrew from any further consideration of such a trial.

v. At the most recent EURAMOS Strategy Group meeting, held June 5th in Chicago, the advised standard chemotherapy on closure of EURAMOS-1 was cisplatin, doxorubicin, methotrexate. A statement included in newsletters sent to all participating centres in 15 countries included the following statement

   Treatment recommendation for future osteosarcoma patients treated outside of trial
   Following the closure to accrual of EURAMOS-1, the Trial Management Group members consider MAP (high-dose methotrexate, doxorubicin, cisplatin), with no adjustment of post-operative treatment based on histological response, to be the standard of care for their patients with newly diagnosed, resectable osteosarcoma. All emerging data from the analyses of EURAMOS-1 will be disseminated to investigators when available. Plans for a further international trial, EURAMOS-2, are in development. MAP will again be the chosen standard treatment arm. In the meantime, inclusion of patients in well designed clinical trials when available is encouraged.
   Source EURAMOS Newsletter July 2011 at www.euramos.org

   An identical position was agreed by the bone subgroup of the National Cancer Research Institute Sarcoma Clinical Studies Group and endorsed by the main CSG in May 2011.

vi. Successor studies to EURAMOS-1 are in development using MAP as standard chemotherapy and testing the addition of other agents.

vii. Emerging evidence from translational studies indicate that for sub populations of patients with osteosarcoma, mifarmurtide may represent a rationale treatment (Buddingh et al, Clin Cancer Research 2011; 17:2110-9) but further validation in prospective clinical trials would be required to determine the clinical relevance of such observations.

viii. Overall, there is considerable dismay within the expert osteosarcoma community that obtaining further robust data to determine the value of mifamurtide is not seen more universally as a priority.

Dr Jeremy Whelan, August 15th 2011