High-grade bone sarcomas with synchronous metastases in patients older than 40: Results of the European Bone over 40: Sarcoma Study (EURO.B.O.S.S.)

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Background: European Bone over 40 Sarcoma Study (EURO.B.O.S.S.) is an European prospective intergroup collaboration for the study of patients older than 40 years with high-grade (HG) bone sarcomas. The results obtained in patients with metastatic disease at diagnosis are here presented.

Methods: Patients with HG Osteosarcoma (OS), HG sarcoma (HGS), Leyomiosarcoma (L), Dedifferentiated chondrosarcoma (DCh), were included into the study. An intensive chemotherapy protocol with cisplatinum, doxorubicin, ifosfamide ± methotrexate combined to surgery was offered to the patients.

Results: Amongst 422 evaluable patients who entered EURO.B.O.S.S., 122 (29%) had metastases at diagnosis, 51 female and 71 male, median age 53 years (41-65). The Lung was the most common site of metastases (86% of patients). skeletal involvement was reported in 26%, 15% had other sites of metastases. The incidence of synchronous metastases differed according to histology (DCh 40%, OS 30%, HGS 22%, L 5%, p = 0.02), site (spine 57%, pelvis 41%, humerus 35%, femur 27%, other 23%, maximal facial 11%, p < 0.02), LDH (high 41%, normal 21%, p = 0.001) serum alkaline phosphatase (SAP) (high 41%, normal 23%, p = 0.005). One toxic death was recorded, 20% of patients had febrile neutropenia, renal toxicity grade 1 to 3 was observed in 26% of patients, neurotoxicity grade 1 to 3 in 16%. Overall survival at 3 and 5 years was 36% (95%CI 24%-47%) and 26% (95%CI 13%-38%), respectively. 5-y OS was 46% (95%CI 21%-72%) in case of surgical complete remission (SCR) and 8% (95%CI 0-21) in patients without SCR (p = 0.001). Survival did not correlate with gender, histology and SAP, but it was influenced by metastatic pattern [5-y OS: Lung only 30% (95%CI 14%-45%), bone only 29% (95%CI 0-63%), multiple sites 14% (95%CI 0-30%), site of primary (5-y OS: spine 0, pelvis 8% (95%CI 0-23%), humerus 0, femur 47% (95%CI 24-69%), other 33% (95%CI 0-87%), maxillofacial 67% (95%CI 13-100%), and LDH (5-y OS: High 0, normal 41% (24%-58%).

Conclusions: Site of primary, histology, SAP and LDH levels correlate with the incidence of metastases at diagnosis. Primary tumor site, metastatic pattern and LDH levels are significant prognostic factors. About 25% of patients older than 40 with metastatic bone sarcomas can be long term survivors thanks to an aggressive strategy of treatment. Any attempt must be done to achieve surgical complete remission.