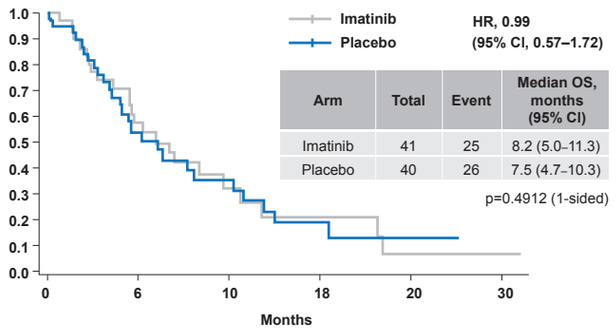
Figure 2. Overall Survival



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Results From the EURAMOS-1 Trial

Written by Maria Vinall

Results from the Combination Therapy, PEG-Interferon Alfa-2b, and Surgery in Treating Patients With Osteosarcoma trial [EURAMOS-1; NCT00134030; *J Clin Oncol* 2013 (suppl; abstr LBA10504)] show that maintenance therapy with pegylated interferon α-2b (PEG IFN-α-2b) after surgery and chemotherapy does not improve event-free survival (EFS) in patients with high-grade osteosarcoma and good response to preoperative methotrexate, doxorubicin, and cisplatin (regimen collectively called MAP).

EURAMOS-1 is a randomized controlled trial from the European and American Osteosarcoma Study Group that investigated the efficacy of maintenance therapy with PEG IFN-α-2b in patients with resectable osteosarcoma and "good response" (<10% viable tumor at surgery) to preoperative chemotherapy. The results were presented by Stefan S. Bielack, MD, PhD, Klinikum Stuttgart Olgahospital, Stuttgart, Germany.

Osteosarcoma is a rare cancer, with 2 to 3 cases per million per year, in which histologic response is a prognostic factor for survival. Poor responders are generally considered to have a 3-year EFS and 5-year overall survival (OS) rate of 45% each [Ritter J, Bielack SS. *Ann Oncol* 2010]. Among good responders, those rates climb to 70%. IFN-α has shown growth inhibition in osteosarcoma cell lines, animal studies have extensively studied it in other tumors as maintenance therapy, and its safety in children is well established. These factors combined with the relatively favorable prognosis for patients with good histologic response may make IFN-α a reasonable option for maintenance therapy.

Patients aged ≤40 years who had resectable localized or primary metastatic high-grade extremity or axial osteosarcoma were eligible for registration at diagnosis, provided they had no pretreatment for osteosarcoma and no prior chemotherapy. All patients received 2 cycles of MAP induction followed by surgical resection. Good histologic responders were then randomized to 4 cycles of MAP alone (MAP group) or 4 cycles of MAP followed by PEG IFN-α-2b weekly from Week 30 to Week 104 (MAP-IFN group). The starting dose of PEG IFN-α-2b was 0.5 μg/kg/week (maximum of 50 μg) given subcutaneously for 4 weeks. If the drug was well tolerated, the dose could be escalated to 1.0 μg/kg/week (maximum of 100 μg). The primary study endpoint was EFS, defined as death, local recurrence, new metastatic disease, progression, or secondary malignancy. Secondary endpoints were OS, toxicity, and quality of life.

A total of 2260 patients were registered between April 2005 and November 2011, which makes it the largest trial studying this rare cancer. Good response was confirmed in 1041 patients, of which 715 (male, 59%; median age, 14 years) consented to randomization (MAP, n=358; MAP-IFN, n=357). Of the 357 patients randomized to the MAP-IFN group, 271 (76%) started treatment with PEG IFN-α-2b at a median of 5.4 months after randomization. The primary reason for not starting PEG IFN-α-2b was refusal (66/86 patients).

Grade 0 to 2 toxicities were reported by 70% (n=187) of patients receiving PEG IFN-α-2b while 30% (n=81) reported Grade 3 or 4 toxicities. Grade 4 toxicities included 13 hematologic, 3 cardiac, and 1 each dyspnea, mood alteration, and amylase. At study end, 37 were still receiving PEG IFN-α-2b while 234 subjects had stopped it (128 had completed therapy; 106 terminated early). Reasons for early termination were toxicity (n=44), disease progression (n=25), and refusal/other (n=37). The median duration of PEG IFN-α-2b therapy was 14.9 months. After a median follow-up of 3 years following randomization, there was no significant difference in EFS between the MAP and MAP-IFN groups (74% vs 77%; HR, 0.82; 95% CI, 0.61 to 1.11; p=0.201).

In conclusion, MAP plus maintenance therapy with PEG IFN-α-2b was not superior to MAP alone, but it should be noted that the results may have been influenced by the failure of 24% of patients to start PEG IFN-α-2b treatment. Further follow-up for events and survival is ongoing.