

Scandinavian experience in classical osteosarcoma

Results of the SSG XIV protocol

Sigbjørn Smeland¹, Øyvind S Bruland^{1,2}, Lars Hjorth³, Otte Brosjö⁴,
Bodil Bjerkehagen⁵, Gustaf Österlundh⁶, Åke Jakobson⁷, Kirsten Sundby Hall¹,
Odd R Monge⁸, Olle Björk⁷ and Thor A Alvegaard⁹

Correspondence: sigbjorn.smeland@medisin.uio.no

¹Division of Cancer Medicine and Radiotherapy, The Norwegian Radium Hospital, Oslo University Hospital, Oslo, Norway

²University of Oslo, Norway

³Department of Pediatric Oncology, Lund University Hospital, Lund, Sweden

⁴Department of Orthopaedics, Karolinska Hospital, Stockholm, Sweden

⁵Division of Pathology, The Norwegian Radium Hospital, Oslo University Hospital, Oslo, Norway

⁶Department of Pediatric Hematology and Oncology, The Queen Silvia Children's Hospital, Sahlgrenska University Hospital, Gothenburg,

⁷Pediatric Oncology Unit, Astrid Lindgren Children's Hospital, Stockholm, Sweden

⁸Department of Oncology, Haukeland University Hospital, Bergen, Norway

⁹Department of Cancer Epidemiology, Lund University Hospital, Lund, Sweden

Background and purpose The Scandinavian Sarcoma Group (SSG) XIV protocol was based upon the organisations experience from 3 previous osteosarcoma trials and was considered best standard of care for patients with extremity localised, non-metastatic osteosarcoma. We report the outcome of this protocol.

Patients and methods From March 2001 to April 2005, 63 patients recruited from 10 centres in Finland, Sweden and Norway were included in this analysis. Patients received pre-operative chemotherapy consisting of 2 cycles of paired methotrexate (12 g/m²), cisplatin (90 mg/m²) and doxorubicin (75 mg/m²). Good histological responders continued with 3 cycles postoperatively whilst poor responders were salvaged with the addition of 3 cycles of ifosfamide (10–12 g/m²). Outcome data was compared to previous SSG osteosarcoma trials.

Results With a median follow-up of 64 months for survivors, the projected metastasis-free and sarcoma-related survivals at 5 years were 69% and 77%, respectively. 84% of the patients were treated with limb salvage surgery (49 patients) or rotationplasty (4 patients). 3 toxic deaths (5%) were recorded, all related to acute chemotherapy toxicity. The 5-year metastasis-free survival of patients receiving salvage therapy was 47% compared to 89% for good histological responders that only received the 3 drug combination postoperatively.

Interpretation Outcome in the SSG XIV protocol compares favourably to previous SSG osteosarcoma

trials and other published trials. The addition of ifosfamide to poor responders as an add on treatment did not improve outcome for poor responders to a similar level as for good responders. In a multi-institutional setting limb salvage surgery can safely be used in more than 80% of the patients.

Current management of high-grade osteosarcoma comprises pre- and postoperative chemotherapy in combination with complete surgical removal of all tumour sites (Link et al. 1986, Fuchs et al. 1998, Bacci et al. 2000). With this strategy, long-term overall survival rates of 70% are reported for patients with non-metastatic, extremity localized (classical) osteosarcoma and more than 80% of the patients are managed by limb-salvage surgery (Bielack et al. 2002, Smeland et al. 2003, Ferrari et al. 2005). Preoperative chemotherapy offers an opportunity to modify postoperative chemotherapy according to histological response. Although never proven effective in a randomized trial, this principle has been used in several osteosarcoma trials (Rosen et al. 1979, Rosen et al. 1982, Winkler et al. 1988).

The active drugs in osteosarcoma are doxorubicin, methotrexate, cisplatin, and ifosfamide, but

