

## Summary

### Radiochemotherapy with weekly cisplatin in the treatment of head and neck cancer.

**Purpose:** The objective of this study was to evaluate the feasibility, toxicity and efficacy of postoperative and definitive radiochemotherapy with weekly cisplatin in locoregionally advanced or high risk head and neck cancer.

**Material and methods:** Patients with head and neck cancer of stage III-IVb or patients with insufficient margins of resection after initial surgery were included in the study of postoperative radiotherapy. Radiotherapy consisted of 70 Gy/ 7 weeks/ 35 fraction after R1/2 resection and 60-64 Gy/ 6-6,5 weeks/ 30-32 fraction after R0 resection, respectively. Patients with head and neck cancer of stage II-IVb without initial resection were included in the study of definitive radiochemotherapy. Radiotherapy consisted of 70 Gy / 7 weeks / 35 fraction. All patients received concurrent cisplatin 40 mg/m<sup>2</sup> weekly.

**Results:** *Postoperative radiochemotherapy:* Between 6/2002 and 12/2008, 100 consecutive patients [WHO ≤ 2, male to female ratio 84/16, median age 54 years] were treated. Tumours of the oropharynx were the most frequent (49%) and stage IV was predominant (86%). 96% patients received the full radiation treatment as planned. Median total tumor dose was 66 Gy. Omission of weekly cisplatin had been occurring frequently, the most frequent reason for its early cessation were hematological toxicities. Grade 3/4 mucosal toxicity developed in 32%. No death was observed during the treatment. The late toxicities were acceptable, predominantly subcutaneous fibrosis and xerostomia in most of the cases. We recorded six cases of osteonecrosis. Two and half year overall survival, locoregional control, time to progression and disease free survival were 64%, 88%, 79% and 59%, respectively. Multivariate analysis revealed that the only prognostic factor for survival was primary surgery at the University centre.

*Definitive radiochemotherapy:* Between 2/2002 and 8/2009, 148 consecutive patients [WHO ≤ 2, male to female ratio 6/1, median age 56 years] were treated. Tumours of the oropharynx were the most frequent (46%) and stage IV was predominant (80%). 89% patients received the full radiation treatment as planned. Median total tumor dose was 70 Gy. Omission of weekly cisplatin had been occurring frequently, the most frequent reason for its early cessation were hematological toxicities. Grade 3/4 mucosal toxicity developed in 32%. 12 deaths were observed during the treatment. The late toxicities were acceptable, predominantly subcutaneous fibrosis and xerostomia in most of the cases. We recorded five cases of osteonecrosis. Three-year overall survival, locoregional control, time to progression and disease free survival were 34%, 60%, 52% and 29%, respectively. Multivariate analysis revealed that negative prognostic factors were N > 2a, smoking status, daily consumption of alcohol, total dose of radiotherapy < 70 Gy, number of chemotherapy cycles ≤ 4.

**Conclusion:** Postoperative and definitive radiochemotherapy with weekly cisplatin is toxic, but tolerable and highly effective in terms of locoregional control and survival. Low renal and gastrointestinal toxicity favor the weekly application over the standard high-dose regimen. A randomized trial is warranted to finally answer the question whether weekly cisplatin adds more substantial benefit to radiotherapy than a three-weekly regimen.