## VHN 06

PRELIMINARY RESULTS OF CIS-PLATIN, VINDESINE, AND ETOPOSIDE IN THE TREATMENT OF ADENOID CYSTIC CARCINOMA OF THE HEAD AND NECK

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Adenoid cystic carcinoma (ACC) is an uncommon slow grading malignant tumor characterized by frequent local recurrences. The majority of ACC arises from the glands of the oral and respiratory tract in the head and neck region. There is only little information on the use of chemotherapy in this tumor entity. Since 1983 we treated 9 pts with advanced ACC with a combination therapy of cis-platin (DDP) 100mg/m² d 1), vindesine (VDS) 3mg/m² (d 1), and etoposide (VP16) 100mg/m² (d 3-5) every 28 days in a total of 4 courses. In cases of intolerable reactions cis-platin was replaced by ifosfamide 1000mg/m² (d 1) under mesna protection. In 7 pts initial therapy consisted of surgery only, the 2 remaining pts, who were considered inoperable received chemotherapy as initial treatment. The group consisted of 7 females and 2 males, age 36 to 75 years. Primary manifestations of the tumor were: orbit, larynx, hard palate, trachea, and parotid gland. One female had undergone surgery and suffered from metastases to the lung only. In 3 cases there was an adverse reaction to cis-platin so that this drug had to be discontinued and ifosfamide was administered. Prior to chemotherapy 6 pts presented with measurable tumor parameters. General staging (CT and ENT-examination, ultrascan abdomen, chest x-ray) was performed before and after therapy. Outcome: CR 2/6, mean duration 23 months. In both pts there was a recurrence of the tumor after 21 and 25 months respectively. In one patient a second CR which is ongoing for 11 months was induced by using same drug regimen. PR 3/6, mean duration 6.7 months. In one patient a progression of the tumor occurred after 7 months. NC 1/6, duration 28 months. After this period, in addition to local recurrence there was progress of the lung metastases. In three pts the primary tumor was subtotally resected. These patients presented no measurable tumor parameter and so far after 10 months observation there is no evidence of recurrence. Conclusions: Preliminary results of this combination therapy for ACC of the head and neck region show a high remission rate. All primary tumors responded to the initial treatment while one patient with distant metastases had no change.

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## VHN 07

CISPLATIN (DDP) AND ETOPOSIDE (VP-16) AS PRIMARY CHEMOTHERAPY IN PATIENTS WITH SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK REGION (SCC-HN).

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Combined cisplatin (DDP) and 5-FU is the most effective chemotherapy in the treatment of squamous cell carcinoma of the head and neck (scc-hn) (Decker et al., Cancer 51:1353-55, 1983; von Heyden et al., Onkologie 7: 183-190, 1984). However, the toxicity and subjective side-effects are severe. To develop better tolerable drug combinations we combined DDP 100 mg/m² iv day 1 with etoposide (VP-16) 120 mg/m² iv days 3-5 every 21 days (1-3 cycles) in a phase II trial. 31 scc-hn patients (pts) with no prior therapy and no distant metastases were treated. Due to severe granulocytopenia in the first 8 pts (group 1), VP-16 was reduced to 80 mg/m² iv days 3-5 in pts 9 to 31 (group 2). In group 1 two CRs, 2 PRs, 2 MRs and 2 NCs were achieved. In group 2 one CR, 5 PRs, 11 MRs, 4 NCs and 2 PDs were noted. The CRs were confirmed by histology. Granulocytopenia was the most important side-effect: 9 pts (4 in group 1, 5 in group 2) developed WHO grade IV toxicity, 4 and 6 pts grade III. Erythropoesis and thrombocytosis were only mildly influenced. Nausea and alopecia were mainly of grades II and III. Compared to the results of previous phase II trials with DDP/5-FU, our experiences with DDP/VP-16 show inferior results. Even when given in a dose where the bone marrow toxicity is severe, the response rates of DDP/VP-16 are lower than with DDP/5-FU.

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## VHN 08

ALTERATIONS OF LYMPHOCYTE SUBPOPULATIONS BY CHEMOTHERAPY AND CHEMOIMMUNOTHERAPY (THYMOSTIMULIN) IN PATIENTS WITH HEAD AND NECK CANCER

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The aim of our study was to evaluate the influence of chemotherapy on the lymphocyte subset distribution in tumor patients and to answer the question if thymostimulin, a soluble preparation of calf thymus, is able to restore chemotherapy induced immunodeficiency.
Patients with primarily inoperable squamous cell carcinoma of head and neck (T3-4/N1/M0) were treated with two cycles of chemotherapy (cis-platinum 100 mg/m² iv (day 1) and VP-16 80 mg/m² i.v. (days 3 to 5)). After the second cycle of chemotherapy 8 out of 20 patients were treated additionally with thymostimulin at a dosage of 1 mg/kg i.m. every day during the first week and then twice weekly. 9 out of 20 patients without additional immunotherapy served as controls.
Lymphocyte subpopulations were determined before, directly after and three weeks after starting every therapy cycle.
Under chemotherapy the number of Okt-11 and Leu-4 positive T-lymphocytes as well as the Okt-4/Leu-3 and Okt-8/Leu-2 subsets decreased slightly without any significant alteration of the T-helper/T-suppressor ratio. In contrast, additional treatment with thymostimulin was accompanied by an marked increase of T-lymphocytes and their subsets. The more pronounced increase of Okt-8/Leu-2 positive cells as compared to the increase of Okt-4/Leu-3 positive cells resulted in an decrease of the T-helper/T-suppressor ratio.

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## VHN 09

RESULTS OF NEOADJUVANT CHEMOTHERAPY IN HEAD AND NECK CANCER

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To improve the unfavourable results in advanced head and neck cancer 26 patients with cancer of oral cavity or oropharynx (stage IV: n=10; stage III: n=7; stage II: n=8; stage I: n=1) obtained the following chemotherapy before surgery: 1 mg vincristine and 400 mg/m² methotrexate on day 1 plus leucovorin and thymidine, 15 mg bleomycin on day 3, 5, 7 plus inosine. If possible, this weekly regimen was repeated 5 times.
The clinical response was evaluated at the end of chemotherapy: CR: n=1; PR (>50% tumor regression): n=16; MR: n=3; NC: n=2; PG: n=4. Overall, a tumor regression was obtained in 20/26 patients (76.9%). Following chemotherapy 4 patients underwent surgery without radiation and 19 patients surgery with subsequent radiation (60 Gy). 17 responders with tumor regression of more than 50% by clinical judgement at the end of chemotherapy were staged before and during surgery. 3 groups were distinguished: improvement of TNM-stage, tumor histologically not detectable (n=5); improvement of TNM-stage, tumor histologically detectable (n=6); TNM-stage unchanged or deteriorated (n=6).
After a follow-up of at least 36 months after chemotherapy 12/26 patients are still alive. 2 of 17 responders (CR and PR) had died without detectable disease. The median survival time (MST) of the responders has not yet been reached. In contrast, in 9 nonresponders (MR, NC and PG) MST is only 15 months although the difference is not significant.
Neoadjuvant chemotherapy using medium-dose methotrexate and bleomycin is not only an effective and well tolerated regimen in head and neck cancer but in case of response may also prolong the survival time.

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