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CHEMOTHERAPY OF METASTATIC MALIGNANT MELANOMA BY CISPLATIN / IFOSFAMID OR CISPLATIN / ACTINOMYCIN D
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Recent results of chemotherapy in patients with metastatic malignant melanoma are not encouraging. Response rates below 50 % and remission duration below 1 year are common results in many studies with different therapeutic agents. DTIC the agent with the greatest number of patients treated with achieved response rates of about 20 % and a remission-duration between 2 and 6 month. We allocated in a non-randomised study 30 patients with metastatic malignant melanoma into two different therapy-arms:

Group A (n=8) Cisplatin 80 mg/m² d.1, Actinomycin D 0.4 mg/m² d.1-d.3 q.d.21. Group B (n=22) Cisplatin 80 mg/m² d.1, Ifosfamid 1.5 g/m² d.1-d.5 q.d.21. 20 men and 10 women entered the study. Median age was 50.6 years (22-75 years). Predominant sizes of metastases were cutaneous 2, lymphonodular 4, visceral 24. Predominant side-effects in group A were medium mucositis and in arm B bone marrow hypoplasia without incidence of febrile episodes.

Results Group A complete remission 1, partial remission 1, minor response 3, no change 1, non-responder 2. Group B complete remission 3, partial remission 10, minor response 3, non-responder 7. Median time of response was 4.1 month in both arms. (1-22 month) The median survival time of patients responding to chemotherapy was 6.7 month while median survival time of patients, who did not respond was 3.5 month. Median number of chemotherapy-courses were 4.

Conclusions The chemotherapy Cisplatin / Ifosfamid seems to be superior to Platin / Actinomycin D. Response is better than in recent studies with DTIC as single agents.

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Ifo 20

IFOSFAMIDE AND ETOPOSIDE AS SECOND LINE THERAPY IN ADVANCED BREAST CANCER
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Salvage chemotherapy in advanced breast cancer patients as second or third line therapy has limited potential. In a review of several monotherapy-trials ifosfamide showed a response rate of 56 % in breast cancer. The good results of the combination chemotherapy with ifosfamide - etoposide in advanced lung cancer encouraged us to start a pilot study with this combination in breast cancer.

12 patients, 3 pre-, 9 postmenopausal, with progressive metastatic breast cancer after different chemotherapy regimens were treated with ifosfamide 1500 mg/m² day 1-5 i.v. and etoposide 120 mg/m² day 3-5 i.v. every 4 weeks. For uroprotection mesna was used. After two chemotherapy cycles the following results were obtained: 4/12 patients achieved PR, no change was seen in 3 patients. 2 patients were not evaluable. Major side effects were: hair-loss in all cases, mild nausea in 9 patients, vomiting in 2 patients, leucopenia <2000/μl in 2 patients. Central-nervous side effects, such as hallucinations and confusions were seen in three patients. In conclusion ifosfamide and etoposide appears to be an effective palliative chemotherapy regimen in advanced breast cancer.

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Ifo 21

IFOSFAMIDE MONOTHERAPY IN TESTICULAR CANCER
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Today, metastasized testicular germ cell tumors are amongst the few solid tumors, that can be cured by polychemotherapy. Retrospectively, we analysed therapy results of 39 pts. with metastasized non-seminomatous germ cell tumors, treated by ifosfamide as a monotherapy from 1970-77. All had measurable tumor parameters, 24 pts. were pretreated by a triple drug combination from LI. The dosage of ifosfamide varied, with an average dose of 11 g/m² per cycle. 8/39 pts. (29 %) achieved CR and 14 (36 %) PR. For 8/14 pts. with a partial remission we achieved NED by salvage LA or thoracotomy, therefore 16/39 pts. (41 %) were free of tumor after chemotherapy and operation. 6 of them survived more than 5 years. This comes up to a curative result of 15 %.

Side-effects were nausea, vomiting and moderate bone marrow toxicity. The mean Nadir-value of leucocytes was 2700, reaching from 40-9200; the mean Nadir-value of platelets was 139000, varying from 36000-349000. Despite an urinary flow of at least 6 l/24h and alkalisation of the urine in 36/39 pts. microscopic haematuria occurred, whereas only 4 pts. complained of cystitis. All pts. with an overall-dose of more than 600 mg/kg body weight showed complete alopecia. One of the pts. evolved a stuporous condition on the third day of therapy, receding completely within 24 hours after discontinuation of ifosfamide. Brain metastases were ruled out.

In 8/39 pts. we achieved a complete remission with ifosfamide monotherapy, further 8 reached an NED-status after operation. 6 pts. with this rapidly progressive tumor survived more than 5 years and can be considered as cured. This advantageous results proves the high effectiveness of ifosfamide for metastasizing germ cell tumors with a curative effect of 15 %.

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Ifo 22

RESULTS OF IFOSFAMIDE TREATMENT IN METASTASIZED RENAL CELL CANCER
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Chemotherapy of metastasized renal cell cancer has been disappointing in the past (S.K. Carter and T.H. Wasserman, Cancer 36, 729, 1975). Since its clinical introduction ifosfamide was administered in 21 patients (13 male, 8 female) aged 34-81 (mean 53,6) years, after previous nephrectomy suffering from multiple metastases in the lungs, bones, liver and lymph nodes. Ifosfamide (Holoxan^R) was applied by i.v. infusion as a monotherapy (20-30 mg/kg = 1,5-3,0g x 10 days) or a polychemotherapy (1,5-2,0g x 3/week) combined with procarbazine 125 mg daily, 5-FU 250 mg x 3/week, MTX 5 mg x 2/week and vinblastine 5 mg/week; additionally antiemetics and mesna (uro-mitexan^R). Total doses of ifosfamide (mean: 2 courses) varied between 15,0-30,0g (monotherapy) and 9,0-18,0g (combination therapy).

Complete or partial remission was observed in 2 resp. 4 patients (6/21=29%) while further 6 patients reached stabilization and in 9/21 patients (=42%) progression took place. Ifosfamide monotherapy resulted with CR in 1/7 patients (14%) while polychemotherapy caused 1 CR+4 PR (5/14 patients=36%). Mean duration of remission differed extremely between CR (54 months) and PR (4,2 months). Survival time in PR+STAB patients lasted 16,7 months (mean). Conclusions: 1) Ifosfamide proved to be of (specific ?) effectivity in renal cell cancer. 2) Regarding remission rates polychemotherapy with ifosfamide turns out superior to monotherapy. 3) Ifosfamide may be provided for adjuvant chemotherapy of renal cancer.

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