Conclusions:
TP-1 can be given safely daily i.m. to man in single doses of 1 mg/kg.

IFOSFAMIDE (IF) WITH THE UROPROTECTIVE AGENT MESNA (MS) IN THE TREATMENT OF SQUAMOUS CELL CARCINOMA OF THE LUNG

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Ifosfamide has been reported to possess a definite activity in non-small cell carcinoma of the lung (Harrison et al. 1979) although its dosage is limited by urotoxicity. This toxic effect can be effectfully prevented by the concomitant use of the uroprotective agent MS (Scheef 1979). The aim of this study is to define the response rate for higher IF-doses under MS-protection. 24 patients (pts) with advanced, histologically or cytologically proved squamous cell ca. of the lung have been treated with IF 1.8 g/m2 iv daily on 5 consecutive days repeated every 4 weeks. MS was given after each IF-dose at 0^h, 4^h and 8^h either iv (0.36 g/m2) or po (0.72 g/m2). No patient had previous chemo- or radiotherapy, all had objectively assessable tumour parameters. A total of 54 treatment courses has been applied. Reversible gross hematuria has been observed in 5/54 courses (9 %), WBC 1'000 - 2'000/mm3 in 15/54 (28 %) and WBC $<$ 1'000/mm3 in 5/54 (9 %). Other toxic effects included generalized weakness, nausea, vomiting and alopecia. Presently 15 pts are evaluable ($>$12 wks) for response (median age: 63; Karnofski 70 - 100). So far 1 CR and 1 PR (CR+PR = 13.3 %) have been noted for a duration of 213+ respectively 68+ days. Nine pts showed NC after 3 courses and 4 were progressive. Since these preliminary data show some activity of IF in squamos cell ca. of the lung, patient accrual will continue. At the schedule used hemorrhagic cystitis is effectfully prevented by MS while leukopenia is the major dose limiting factor in this previously untreated population.

COMBINATION HORMONOTHERAPY WITH TAMOXIFEN AND FLUOXYMESTERONE IN PATIENTS WITH ADVANCED BREAST CANCER RELAPSING ON HORMONOTHERAPY

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Twenty-six patients were treated with a combination of tamoxifen (TAM) and fluoxymesterone (10 mg t.i.d. each) after disease progression on prior hormonotherapy (HT) (in only two cases prior HT did not include TAM). The patient population was characterized by a high median age (65 years, range 41 to 82 years) and by a high median time interval between diagnosis and entry into the trial (4,5 years, range 10 months to 25 years). Five of 19 patients (26 %) exhibiting a partial response (PR) or stable disease (NC) on previous HT responded to the combination (median time to relapse 7 months, range 3 1/2 to 17+ months). Nine patients (47 %) maintained NC (median duration 5 months, range 1 1/2+ to 9 1/2 months). Six non-responders had subjective improvement with a median duration of six months although two of these patients had objective progressive disease (PD). No response has been seen in seven patients who experienced PD during prior hormonal manipulation or who were non-evaluable for response to prior HT. Median overall survival was 10+ months (range 2 1/2+ to 19+ months): 17+ months for responders (6 to 18+ months), 8+ months for patients with NC (2 1/2+ to 19+ months, all alive) and 10+ months for patients with PD (3+ to 17+ months). The drug combination was well tolerated with virilization, weight gain and hemoglobine increase as predominant side effects. Based on our findings the role of combination HT as a secondary endocrine manipulation in metastatic breast cancer is discussed.

THE MODIFICATION OF EXPERIMENTAL PANCREATIC CANCER BY DIETARY FAT

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Dietary fat has been implicated in the development of human pancreatic cancer. Since the pancreatic cancer model developed by us shows remarkable similarities to pancreatic cancer in man in its biological and morphological patterns, we tested the effect of dietary fat on the induction of pancreatic cancer with an experimental design in order to determine in which phase of carcinogenesis (initiation or promotion) dietary fat is effective. A semisynthetic diet of corn oil was fed at three levels (4.5, 9.0 and 18.0 gm/385 Kcal) to Syrian golden hamsters either before (3 - 8 weeks of age) or after (8 weeks until death) single treatment with a pancreatic carcinogen. The high fat diet enhanced the incidence, multiplicity and size of pancreatic tumors when fed after carcinogen treatment, especially in male hamsters. However, the level of fat fed before carcinogen treatment appeared to have little effect on pancreatic