Bre 07**CHARACTERIZATION OF A MONOCLONAL ANTIBODY AGAINST MEDROXYPROGESTERONE ACETATE (MPA)**

H.C. Blosssey, H.E. Wander, S. Lichter*, F. Kohen*, J. Köbberling, G.A. Nagel

Investigation of the pharmacokinetic and pharmacodynamic basis of the therapy of metastatic breast cancer with high dose MPA has provided significant insight into the mechanisms of the antitumor activity of the drug. We have developed a monoclonal antibody against MPA which did not crossreact with estradiol, estrone, progesterone, 17 α -hydroxyprogesterone, androstendione, dehydroepiandrosterone, testosterone, cortisol, and aldosterone. In comparison with a polyclonal kindly provided by the Upjohn Comp., Kalamazoo, MI, the monoclonal showed the following specifications: specific and unspecific binding of MPA was 18% and 10%, respectively, with the monoclonal, 30% and 16% with the polyclonal. MPA plasma concentrations were 2-10 times lower with the monoclonal than with the polyclonal. During oral administration of MPA 2x500 mg/day, MPA in plasma decreased after the first dose to about 30% within 12 hours. The lowest MPA plasma level coinciding with a complete suppression of endogenous cortisol secretion was about 60 ng/ml. During therapy with MPA 1000 mg/day p.o. plasma concentrations usually reached or exceeded 100 ng/ml. The classical pharmacokinetic characteristics for high dose MPA therapy using a polyclonal (H.C. Blosssey et al., Cancer Chemotherap. Pharmacol. 8, 77, 1982) could essentially be confirmed using the monoclonal antibody against MPA.

Medizinische Klinik der Universität, Robert-Koch-Straße 40, D-3400 Göttingen; *Department of Hormone Research, The Weizmann Institute of Science, Rehovot 76100, Israel.

Bre 08**LOW-DOSE AMINOGLUTETHIMIDE IN TREATMENT OF POSTMENOPAUSAL ADVANCED BREAST CANCER**

K. Höffken, A.A. Miller, B. Miller, B. Hoffmann, R. Becher, E. Aulbert, B. Schoetensack, G. Schimmel, R.B. Schilcher, R. Callies and C.G. Schmidt

In a phase II study, 31 evaluable patients (pts) with advanced progressive breast cancer (BC) were treated with low-dose aminoglutethimide (AG) (2 x 250 mg per day) without hydrocortisone (HC) supplementation. Mean age of the pts was 60 years (range 42-79) and mean Karnofsky performance status was 80% (range 70-100%). Partial remissions (PR) were observed in 7 pts (23%) with a mean duration of 10+ (range 1.5-15+) months and disease stabilisations (NC) in 10 pts (32%) lasting 2-18+ (mean 6+) months. Bone metastases responded well with 67% PR and NC, whereas locoregional and pleuropulmonary metastases showed disease progression in 54% and 70% of the pts, respectively. There was no significant difference in response rates of pts with positive and unknown receptor status. Of the 2 pts with negative receptors, 1 showed PR, 1 progressive disease. Recorded side effects (drowsiness, ataxia, rush) were mostly mild and transient and did not require drug discontinuation. In 70% of the pts no side effects were observed. Serum estradiol decreased significantly whereas cortisol levels remained unaltered. When compared with conventional-dose AG (1 g per day), low-dose treatment resulted in only a 30% reduction in plasma AG-levels (6.5 vs 4.5 μ g/ml AG after 1 week of treatment). It is concluded that low-dose AG is as efficient as conventional-dose AG in terms of both remission rates and remission duration in postmenopausal BC. Dose reduction significantly decreases incidence and degree of side effects. HC supplementation is not mandatory, either for increase in efficacy or for decrease in side effects of the treatment.

Innere Universitätsklinik u. Poliklinik (Tumorforschung), Westdeutsches Tumorzentrum, Hufelandstr. 55, D-4300 Essen

Bre 09**AMINOGLUTETHIMIDE (AG) IN ADVANCED BREAST CANCER (BC)-LOW DOSE VS STANDARD DOSE** H.J. Illiger, H. Caffier, H. Carterier, B. Eggeling, J. Hartlapp, G. Hartwich, E.U. Kätzlitz, R. Katz, H. Klasen, A.C. Mayr, J. Preiss, K. Rieche, W. Wellens.

AG administered in the standard dosage of 1 g/day, is an effective treatment of advanced BC in postmenopausal women. It has long been presumed that it exerts a hormonal effect on tumour growth by blocking the desmolase enzyme system. A further important effect seems to be inhibition of the peripheral aromatase enzyme system. Experimental studies show that this effect can be achieved at a lower dosage. We compared the clinical benefits and sideeffects of AG at dosages of 500 mg (Group A) and 1 g (Group B) in a Phase III study. In both groups replacement with cortisone acetate is given (50 mg/day). Up to now 109 pts have been randomly allocated to treatment (A: 53, B: 56). There are no significant differences between the two groups with respect to the stratification criteria. So far 71 pts are evaluable for therapeutic result (A: 33, B: 38) and 83 pts for sideeffects (A: 37, B: 46). Up to now we have seen 1 CR and 4 PR in Group A and 7 PR in Group B. Further 20 pts in Group A and 27 pts in Group B show minor response or stable disease. 14/32 in Group A and 16/30 pts in Group B obtained pain relief or freedom from pain ($p > 0.05$). There is also no difference between the two groups in duration of response. Sideeffects were seen in 14 pts in Group A and 21 pts in Group B. Subjectively unpleasant neurological and psychic unwanted effects (tiredness, drowsiness, ataxia and dizziness) were more frequently observed at the high dosage (11 as compared with 3 pts) and the grade of toxicity was more favourable at the lower dosage. Endocrinal sideeffects were rarely observed (1 hypothyreosis in each group and 1 cushingoid in Group B). The results show that low dose AG is as effective as the standard dosage but less toxic.

Städt. Kliniken, Onkologische Abteilung, D-2900 Oldenburg

Bre 10**Results of a Four-year Prospective Randomised Study of Operable Breast Cancer**

R. Kolb, K. Kühnl-Brady, R. Jakesz, K. Moser, H. Rainer, G. Reiner, M. Schemper and J. Spona.

The effect of operative methods, chemotherapy (B) and immunotherapy (C) on a group of 214 patients with stage 1 and 2 breast cancer was investigated by comparison with control group. Stratification was carried out according to climacteric stage, T and N distribution, and the axillary lymph nodes were investigated intraoperatively using frozen sections. Patients in therapy groups B and C received 5-Fu, Metotrexate and Velbe, patients in C an unspecific immunostimulation. Peripherally located T1 or T2 tumours were operated using conservative or modified radical surgery, while patients with positive lymph nodes and negative apices were given either radical or modified radical surgery. In the case of centrally located tumours with negative axilla, modified radical mastectomy was carried out, and positive apex lymph nodes required classical radical operation. Of the 241 patients with a mean observation time of 48 month, 9.5% had local recurrence and 19.1% metastases. Of the conservatively operated women 14.7% had local recurrence and 11.8% metastases. Only 3.2% of the patients with modified radical mastectomy suffered from recurrence ($p < 0.05$). There was no statistical difference between patients who had been given a radical or modified radical operation. After four years there was no statistically significant difference between the control group and B and C. However, the survival rate of patients with hormone receptor-negative grade 3 tumours with chemotherapy improved by about 50%.

1st University Clinic of Surgery, A-1090 Vienna.