*I - i

I - j

A RANDOMIZED PHASE II STUDY COMPARING AMINOGLUTETHIMIDE vs. TRILOSTANE vs. MPA vs. HYDROCORTISONE: AN E.O.R.T.C. STUDY.

C.Rose, H.T.Mouridsen, J.Wildiers, R.Paridaens, R. Sylvester and N.Rotmensz.
The Finsen Institute, Copenhagen, Denmark.

It is of clinical importance to evaluate the relative efficacy and toxicity of the various possibilities for second-line endocrine therapy of postmenopausal patients with advanced breast cancer. From Oct.83 to Nov.85 191 patients were randomized to AG+H: aminoglutethimide (1000 mg) and hydrocortisone (40 mg) vs. MPA: medroxyprogesteroneacetate (300 mg) vs. T+H: trilostane (960 mg) and hydrocortisone (40 mg) vs. H: hydrocortisone (40 mg). So far 134 patients have been assessed and found to fulfill the eligibility criteria: Postmenopausal status; ≤ 75 yrs. of age; measurable and/or evaluable disease (UICC); ER positive or unknown tumours; performance status ≤ 3; one prior course of endocrine therapy except those used in this study. The response to treatment until now has been determined for 102 fully evaluable pts. and was the following for the AG+H (N=27), the T+H (N=23), the MPA (N=27), and the H (N=25) groups, respectively: PD: 67, 78, 63, and 80%; NC: 19, 22, 37, and 16%; PR: 15, 0, 0, and 4%. (P=0.07). The median values for time to progression were 3.5, 3.2, 2.8, and 2.8 months in each of the 4 groups. Side effects were more pronounced in the T+H treated group of pts., the most common of them being nausea and diarrhea.

I - k

STEROID RECEPTORS AND ANTISTEROIDAL AGENTS IN THE TREATMENT OF (HUMAN) PANCREATIC CARCINOMA

P.J. Johnson
Liver Unit, King's College Hospital School of Medicine and Dentistry, Denmark Hill, London SE5 9RS, U.K.

Highly specific, high affinity, oestrogen binding has been detected in nuclear and cytosolic fractions of 8 out of 9 samples of pancreatic carcinoma tissue, but not in normal pancreatic tissue. The binding characteristics were similar to those found in classical sites of oestrogen action such as breast and uterus. The sex hormone metabolising enzymes, aromatase and 5 reductase were also found in pancreatic tumour tissue with activities of the same order as those found in uterus and prostate respectively. This led to an investigation of the effects of hormone manipulation on the growth of human pancreatic carcinoma xenografts in nude mice. Three pancreatic tumour lines, of varying degrees of differentiation and growth rate, each having demonstrable cytosolic oestrogen receptors and high activities of aromatase and 5 reductase were used. The experiments showed that the anti-androgen cyproterone acetate significantly reduced the rate of growth when compared to untreated animals. The anti-oestrogenic agent, tamoxifen was ineffective but the xenografts, unlike tumours in the human, did not contain the nuclear oestrogen receptor. We are currently undertaking a randomised prospective controlled trial of hormonal manipulation in patients with pancreatic carcinoma. To date 112 patients have been entered and randomised to receive either tamoxifen (20 mg b.d.) or cyproterone acetate (100 mg t.d.s.) or supportive treatment only.

I - l

AMINOGLUTEHIMIDE IN THE TREATMENT OF PROSTATIC CARCINOMA: A REVIEW

Mr. M.R.G. Robinson

Aminoglutehimide was initially used in the 1960's as an anticonvulsant until it was withdrawn because of severe endocrine disturbances, including adrenal suppression. It inhibits the adrenal production of Aldosterone, Cortisol and Androgens. It has been suggested that this suppression of the adrenal gland by Aminoglutehimide may be beneficial as a "medical adrenalectomy", in the management of metastatic carcinoma of the prostate which has relapsed on conventional hormone therapy. Several studies have reported subjective and objective responses. This paper reviews the published results and evaluates the role of Aminoglutehimide in the management of prostatic cancer.