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TREATMENT OF ADVANCED PROSTATE CANCER WITH BUSERELIN (HOE 766):A PILOT STUDY

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Gn-RH (LH-RH) analogues have been recently introduced as endocrine therapy of advanced prostate cancer. We treated in a pilot clinical trial 21 consecutive pts with the analogue Buserelin.Nineteen pts are evaluable for response and toxicity.According to the NPCP criteria of evaluation we observed PR in 9 pts(47.6%) and PRO in 10 pts(52.6%).We observed no CR and STAB categories of response. Approximately one half of the pts reached PRO within 14 months of treatment (median 9 months,range 3-14);the other half is in maintained PR at a median follow-up time of 20 months (range 9-30). Treatment was well tolerated the side effects of major complain being impotence and hot-flushes.
Buserelin proved to be effective, at th dosage administered in reducing testosterone levels within castrate range.

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SIMULTANEOUS ADMINISTRATION OF AN LUTEINIZING HORMONE RELEASE HORMONE AGONIST AND DIETHYLSTILBESTROL IN THE INITIAL TREATMENT OF PROSTATIC CANCER.

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It is well known that the first administration of luteinizing hormone release hormone analogues (LHRH A) induces an initial increase of luteinizing hormone (LH) release and a subsequent rise of testosterone (T). This rise is maximal after 3-4 days and is followed by a steady fall of LH and T. Several investigators have reported flare-up symptoms in patients with advanced prostatic cancer, associated with the rise of T, when treated by LHRH A alone. In order to prevent these flare-up symptoms we treated 20 patients with advanced prostatic cancer with an association of a LHRH A (Zoladex Depot®) and diethylstilbestrol (DES) 1 mg/day. DES was given for 14 days, starting 7 days before the first Zoladex Depot injection. T levels fell to near castrate levels within a few days, but rose again 3-4 days after the administration of the LHRH A, to pretreatment values before reaching subsequently castrate levels. No clinical flare-up manifestations were recorded.
We conclude that combination treatment with DES can prevent the flare-up symptoms induced by LHRH A in patients with prostatic cancer.

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STUDIES ON A NOVEL ANTIANDROGEN: ICI 176334

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There has been an urgent need for the development of new antiandrogens which act peripherally. Compound ICI 176334 (Anti-A) appears to fulfil this requirement. Using sucrose density and hydroxylapatite assays, Anti-A inhibits the binding of [^{3}H]mibolerone to androgen receptors in the accessory sexual glands of male rats, but not in the hypothalamis or anterior pituitary. Unlike flutamide, Anti-A suppresses the morphology and function of the rat ventral prostate, but has no influence on the hypothalamus and anterior pituitary. Distribution studies on [^{3}H]-Anti-A indicate that it is concentrated in the prostate and seminal vesicle, but not the hypothalamus. Anti-A inhibits the uptake of [^{3}H]testosterone into the prostate but not the hypothalamus; it has no influence on the tissue distribution of [^{3}H]cortisol or [^{3}H]-oestradiol-17β. Using a variety of biochemical criteria, Anti-A appears to be 5-6 times more active *in vivo* than current antiandrogens, such as flutamide. Whereas flutamide potentiates the release of lutropin and testosterone, Anti-A does not. Our evidence suggests that Anti-A acts peripherally and raises new hopes for successful chemotherapy of prostatic cancer.

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EFFECTS OF FLUTAMIDE ALONE AND FLUTAMIDE PLUS ORCHIECTOMY ON PROSTATIC SIZE AND MALE SEX HORMONES IN PATIENTS WITH PROSTATIC CARCINOMA.

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In order to assess the clinical efficacy of Flutamide (F.) we treated 29 Pts with cancer of the prostate.Pts were randomized to receive either F plus orchiectomy or F alone. The results showed a good responce in the group treated by F plus orchiectomy.In the group treated by F alone we got different results from studies reported elsewhere:testosterone (6.2±3.4 to 5.7±2.6ng/ml) showed steady levels and LH (16.6±9.7 to 26.9±19.3mIU/ml) slightly encreased.Surprisingly the correlation between testosterone and LH became inversely proportional if each group of Pts is considered separately.The Pts with highest testosterone and lowest LH levels has a better response to the treatment,Whereas the Pts with lowest levels of testosterone and highest LH levels has poor benefits from the treatment.This is also partially true with respect to the levels of testosterone in the Pts treated by orchiectomy plus F:the Pts in complete remission has the highest levels of testosterone among this group. The meaning of these results is,from our point of view,related to the competition between testosterone and antiandrogen in the target tissues.Then the testosterone levels might be usefull to control inversely the efficacy of the treatment.