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MEDICAL vs SURGICAL ORCHIECTOMY IN ADVANCED PROSTATIC CANCER

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118 patients were randomized with 62 patients into the long acting D-TRP-6-LHRH (Decapeptyl) group and 56 patients into the orchiectomy group. The mean time to castrate levels of testosterone in the D-TRP-6-LHRH group was 17 days. 50 patients (80%) in the D-TRP-6-LHRH group and 44 patients (78%) in the orchiectomy group had partial remission or stable disease at 3 months. Ten patients in the D-TRP-6-LHRH group and 9 patients in the orchiectomy group have died. There was no significant difference between the groups for response or survival. 3 patients in the D-TRP-6-LHRH group had a disease "flare" in the first 10 days of treatment. The flare symptoms in all patients resolved by the end of 8 weeks. Psychological tests indicated that there was slightly decreased morbidity in the D-TRP-6-LHRH group. Our results indicate that medical orchiectomy offers a safe and highly effective alternative to surgical orchiectomy.

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SUSTAINED SUPPRESSION OF PITUITARY AND TESTICULAR FUNCTION BY CONTROLLED RELEASE INJECTABLE NAFARELIN.

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Synthetic LHRH agonistic analogs are used in the treatment of prostate cancer for suppressing pituitary and testicular function. A controlled release injectable (CRI) formulation was prepared by encapsulating nafarelin in microspheres of polylactic/glycolic acid. Nafarelin CRI, 4 mg, was given to 12 normal volunteers (aged > 50 yrs) by deep IM injections of microspheres loaded with 2%, 4% and 7% nafarelin. Serum FSH, LH and testosterone (T) increased transiently, and then decreased within 2-3 weeks to mean nadir (± SEM) levels shown below:

	FSH (mIU/ml)	LH (mIU/ml)	T (ng/ml)
Baseline	12.8 ± 2.6	7.8 ± 0.5	4.3 ± 0.40
2%	3.1 ± 1.6	2.6 ± 1.1	0.06 ± 0.01
4%	5.6 ± 0.4	2.7 ± 0.1	0.11 ± 0.01
7%	6.3 ± 0.6	2.6 ± 0.5	0.08 ± 0.02

Serum T levels remained suppressed (<0.5 ng/ml) between 26-68+, 26-68, and 19-43 days after the 2%, 4% and 7% loading levels, respectively. There was no response of FSH or LH to 100µg LHRH given IV on day 29. Nafarelin serum levels, measured by a specific RIA, peaked earlier with the higher loadings. No adverse reactions were observed. We conclude that nafarelin CRI completely suppresses pituitary and gonadal function with an exceptionally long duration of action. The properties of this formulation of nafarelin could be of high clinical utility in the treatment of prostate cancer.

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U.K. Trials for treatment of M1 Prostatic Cancer

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Two trials will be presented and discussed:-

I. depot-"Zoladex" v: orchidectomy
(entry closed 31 January 1985)

This study recruited 358 patients from 17 urological centres. 325 patients were evaluable with treatment randomisation as 162 ("Zoladex" 3.6 mg. monthly) and 163 (orchidectomy) with similar demographic features of both arms. Assessment of subjective, objective, endocrine (LH and testosterone), physiological, survival, and other data led to the conclusion that depot "Zoladex" and orchidectomy are equivalent treatments for M1 prostatic cancer.

II. CPA v: depot "Zoladex" v: CPA + depot - "Zoladex"
(ongoing study)

This multicentre study follows on from Study I to examine the action of cyproterone acetate (CPA) 100 mg. t.d.s. as adjuvant to testicular suppression with depot "Zoladex" 3.6 mg. monthly. Criteria for entry, assessment and evaluation are as for Study I. Interim results will be reported.

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PSA ASSAYS IN PROSTATE CANCER

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Prostate specific antigen (PSA) was assayed retrospectively in 131 prostate cancer patients aged 48-87 yr (median 68). Survival ranged from 1 mo-11 yr. Normal PSA level determined by RIA from 61 controls was <5ng/ml. Pretreatment levels at primary tumor diagnosis: stages B&C: 13/16 >5ng/ml(81%); stage D(1&2): 27/28 >5ng/ml (96.5%). During the disease course (treated pts) at discovery of metastasis: 12/17 >5ng/ml(70.5%) To determine the value of PSA assays when physical exams were negative, 52 pts were reevaluated at a max. interval of 12 mo. as a function of their initial PSA concentration:

1st phys. exam neg.	Second physical exam. Positive	Negative	TOTAL
PSA < 5 ng/ml	0	32	32
PSA > 5 ng/ml	11	9	20
TOTAL	11	41	52

$X^2 = 19$ $p < 0.001$

When the initial PSA was negative, there was no clinical evolution during the 1st 6 mo. (3-12); when the PSA was positive, pts had a 55% risk (11/20 cases) of disease progression in the next 4 mo. All PSA assays were coupled with PAP dosage. The specificity of PSA for various cancers was also studied: this prostate cancer marker is not absolutely specific for cancer as elevated values were seen in GI and metastatic breast cancers (23% of cases). PSA sensitivity was 80-96% depending on the initial stage. No PAP values were positive when PSA was negative. PSA anticipates the clinical course by > 3 mo.