1

SUBJECTIVE RESPONSE CRITERIA

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In this paper a number of guidelines are proposed for the assessment of subjective response and quality of life in prostatic cancer clinical research. A review of currently available measures of subjective response (i.e., performance status and treatment toxicities) suggests that the Karnofsky Performance Status Scale and the subjective elements of the W.H.O. Acute and Subacute Toxicity Scales yield the highest levels of validity and reliability, and thus are the instruments of choice. As both measures are widely employed in clinical research, there should be few difficulties anticipated in calling for their routine inclusion in prostatic cancer research. Despite this recommendation, however, further developmental work is required to improve the precision of these measures.
In the case of quality of life assessment, there does not appear to be a clear choice among available measures. While there are a number of promising instruments, none has yet to undergo sufficient field testing to justify widespread adoption in clinical trial settings. In lieu of such a specific recommendation, a number of general guidelines are proffered regarding quality of life instrument development and research implementation.

2

IDENTIFICATION OF THE THREE PREDOMINANT PROSTATIC-SECRETED PROTEINS AND THEIR IMMUNOHISTOCHEMICAL LOCALIZATION IN NORMAL, HYPERPLASTIC AND NEOPLASTIC PROSTATIC TISSUE.

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Prostatic acid phosphatase (PAP), prostate specific antigen (PSA)= α -seminoprotein, and β-microseminoprotein (β-MSP) = β-inhibin, were identified to be the three predominant proteins secreted by the normal human prostate gland. Immunohistochemical localization of these proteins in the normal prostatic acini and ducts with the avidin-biotin complex (ABC) procedure demonstrated each PAP-immunoreactive epithelial cell to be invariably immunoreactive with PSA- and β-MSP-monospecific antisera. The tissue distribution of PAP, PSA, and β-MSP was also examined in a series of 40 prostatic adenocarcinomas, graded according to the WHO-system. Well differentiated tumours (grade I) contained an almost equal number of PAP-, PSA-, and β-MSP-immunoreactive cells. The number of PAP-, PSA- and β-MSP-immunoreactive cells was lower in the moderately and poorly differentiated tumours (grade II-III). The PAP-immunoreactive cells were less frequent than PSA- and β-MSP-immunoreactive cells in grade II-III tumours. The almost identical tissue distribution of PSA and β-MSP in grade II-III tumours suggests β-MSP and PSA to be more sensitive tumour markers for the monitoring of prostatic carcinoma than PAP.

3

ADVANCED PROSTATIC CANCER TREATED BY AN LH-RH AGONIST

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The trial drug was ICI 118.630 (Zoladex). Inclusion criteria: histologically confirmed advanced prostate cancer (T>2 or M1), life expectancy>3 mo., no previous radiotherapy, orchiectomy, chemotherapy. Treatment started in Nov. '84: 30 patients (pts) are evaluable with a follow-up $\geq$ 72 wk (9 pts), $\geq$ 48 wk (7 pts), $\geq$ 12 wk (14 pts); data were updated to end of March 87; mean age 67.9 yr (53-83). Subjective response was evaluated by a mean symptom score using various items (daytime micturition, nocturia, dysuria, hesitancy, flow) and the score of 3 different items: patient activity, bone pain and use of analgesics. Only 3/30 pts showed a permanent positive subjective response. Four different objective responses (complete, partial, stable disease, progression) were possible after evaluating the T category, tumor dimensions, metastasis, plasmatic acid phosphatases. Testosterone (T) and plasmatic LH levels rose after administration; T dropped below the castration level (1ng/ml) some days and remained constantly low. The rate of progressive disease was 21%; disease control was possible in 80% (PR or SD); 1 pt died after 10 wk of therapy of rapidly progressive renal failure. In conclusion, our preliminary results confirm the possibility of offering pts a therapeutic option that can give satisfactory results without psychological problems (orchidectomy) or life-threatening complications typical of more traditional hormonal approach.

4

CLINICAL AND ENDOCRINOLOGICAL RESULTS OF SHORT TERM ANANDRON TREATMENT

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We evaluated the anti-androgen effect of Anandron[R] 150mg b.i.d. for 8 weeks in 16 genetic and endocrinological normal males who opted for male-to-female gender reassignment treatment. Body weight, bicipital adipose fold, blood pressure and pulse rate did not change. All pts experienced some gynecomasty. Hair growth score, hair weight and hair count decreased slowly over the treatment period. Ultrasonographic measurement showed no decrease of the prostate volume. Serum levels of oestron oestradiol, testosterone, andro-stenedione, DHEA, and DHEA-S increased more than twofold. SHBG increased from 1.0 ± 0.12 to 1.89 ± 0.34 mcg%. Serum prolactin levels increased slightly. Basal serum levels of LH increased (5.2 ± 1.1 to 12.2 ± 3.6 U/l), but basal serum FSH levels showed no change. The LH response on LHRH(100ug iv) increased significantly(1553 ± 865 to 3650 ± 740 U/l) whereas the FSH response did not differ. The LH pulse frequency and amplitude increased significantly (resp. 4.4 ± 2.4 to 6.6 ± 1.1/7h and 3.1 ± 0.6 to 4.5 ± 1.2 U/l). We conclude that Anandron[R]: 1) is a clinically effective anti-androgen for reduction of hairgrowth 2) shows no effect on body weight, blood pressure, pulse rate and prostate volume 3) increases LH pulse frequency and amplitude, basal LH level and LH response to LHRH, 4) has no effect on basal FSH level and FSH response to LHRH.