57

METASTASIS AND HORMONE SENSITIVITY

P.M. Martin
Laboratoire de cancérologie Expérimentale
Faculté de médecine Secteur Nord, 13326
Marseilles Cedex, France

The survival rate for patients with solid tumors has not varied notably over the past decades despite the optimization of therapy protocols. These treatments prolong survival and improve the quality of life, but they do not prevent death, which is the consequence of metastatic spread. The prognosis for cancer is thus linked to the tumor's metastatic potential. It thus appears essential to understand the mechanisms of metastasis. Clinical practice and the study of animal models have demonstrated that metastasis results from the expression and amplification of tumor cell populations with a particular phenotype: the metastatic phenotype, whose expression is independent of, but does not exclude, other cell phenotypes. Two main questions require attention:

A) Is the metastatic process random or selective?

B) Is the metastatic process an adaptation of the cellular phenomenon to the involved organ?

The responses to these questions condition the validity of the criteria defined for hormone sensitivity and maintenance of a therapeutic response.

58

PHASE II TRIAL OF D-Trp-6-LH-RH (SUSTAINED RELEASING FORMULATION) IN ADVANCED PROSTATIC CANCER

G. Mathé, R. Keiling, J. Gastiaburu, G. Prévot, J.M. Vannetzel, R. Despax, C. Jasmin, F. Lévi, M. Musset, P. Ribaud and J.L. Misset. SMST & ICIG, Hop. Paul-Brousse, 94-Villejuif, France.

39pts with histologically confirmed prostate cancer have been treated with sustained release formulation of D-Trp-6-LH-RH (SRF). The pts received a daily s.c. injection of 500mcg of immediate formulation D-Trp-6-LH-RH (IF) followed by an i.m. injection every 28 days of SRF, releasing daily 100mcg. Median age was 70 years (58-83). Thirty-one/36pts were heavily pretreated; 36pts (32 stage D, 2 stage C and 2 stage B) are evaluable after 3 months therapy; 3pts are not evaluable because of protocol violation; 6 had progressive disease. SRF induced a marked decrease in LH and testosterone levels. Antitumor action was evaluated on: a) subjective manifestations: urinary symptoms, which improved in 15/24pts (62%) and bone pain in 11/16pts (69%), b) objective measurements: prostatic size evaluated by transabdominal ultrasonography was normalized or reduced in >50% in 3/12 (25%) and by<50% in 5/12pts (41%). Prostatic acid phosphatase regressed to normal in 2/8pts and to >50% in 28pts. Bone scan showed a marked improvement in 3/18 (16%) pts. Six pts progressed under treatment. In a previous study of (IF) D-Trp-6-LH-RH the median duration of response in responders was slighly inferior to one year. We conclude that the SRF is active as the IF. Thus we recommend it to improve local tolerance and acceptance of the treatment.

59

THE ROLE OF PREMALIGNANT LESIONS IN THE DEVELOPMENT OF PROSTATIC ADENOCARCINOMA

J.E. MCNEAL, M.D.
Stanford University Medical Center
Division of Urology
Stanford, California, U.S.A.

Dysplasia in the prostate is a specific intraductal cytologic abnormality having several features resembling those of invasive cancer. Dysplasia is found with increased frequency, extent and severity in prostates which also show invasive carcinoma. Occasionally direct transition from dysplasia to microscopic foci of invasive carcinoma can be found. This premalignant change is found occasionally in prostates from men in the third decade. The morphologic abnormality in dysplasia is consistently accompanied by biologic alterations, evidenced by loss of normal lectin binding. Immunoperoxidase stains using five differentiation antigens indicate that loss of regulation of cell differentiation is a feature of dysplasia.

60

ZOLADEX: ENDOCRINE EFFECTS, EFFICACY AND SAFETY IN ADVANCED PROSTATE CANCER. A FRENCH COOPERATIVE STUDY

R.Metz,M.Namer,L.Adenis,B.Audhuy,R.Bugat,P.Colombel,J.Couette,P.Grise,R.Khater,B.LePorz,G. Levin,P.Marti,M.Mauriac,A.Rouxel,R.Tetelboum
Centre Alexis Vautrin,Nancy, France

From April 84-May 86, 129 patients,mean age 72 yr (45-94)with advanced prostate cancer (124 M1, 5 M0) received subcutaneous injections every 4 wk of a new LHRH agonist, Zoladex Depot 3.6 mg (ICI 118630). Primary tumor histology: 17 G1, 62 G2,38 G3, 12 Gx. Endocrine effects: 4 weeks after treatment initiation, mean serum LH and FSH were suppressed below pretherapy levels and mean serum testosterone (T) was in surgical castrate range. Serum T remained suppressed for as long as therapy was given (max. follow-up 84wk). Objective response: 105 pts evaluable at 3 mo.: 68(65%) partial response; 12(11%) stable disease; 25(24%) progressive disease. Median time to progression 37 wk. 85 pts were symptomatic and evaluable for response at 3 mo: 48(56%) had subjective response as per protocol criteria and 67(79%) in clinician's judgment. Safety: Zoladex Depot was very well tolerated. Major side effects were linked to endocrine effects: decreased libido(92%), decreased erections(86%), hot flushes(48%), breast swelling(3%), breast tenderness. 8 pts had transient increased bone pain and 2 had rapidly progressive skeletal metastases suggesting a flare phenomenon. Conclusion: Zoladex is a safe and effective treatment for advanced prostate cancer.