21

ORCHIDECTOMY VERSUS BUSERELIN IN COMBINATION WITH CPA FOR 2 WEEKS OR CONTINUOUSLY IN THE TREATMENT OF METASTATIC PROSTATE CANCER (EORTC 30843).

HJ de Voogt and members of the EORTC-GU-group.
Dept. Urology, AZVU, Amsterdam.
EORTC Data Center Brussels.

This prospective randomized phase III trial compares orchidectomy as standard hormonal therapy of advanced prostatic cancer, with LHRH-agonist Buserelin, administered as nasal spray 3 dd 400 µg, combined with cyproterone acetate (CPA) 3 dd 50 mg for 2 weeks initially to prevent disease flare-up, or continuously as complete androgen blockade.
The trial,having recruited over 360 patients, is closed to entry in September '89. Stratification of patients for Performance and Metastatic status preceded randomization in the 3 arms mentioned. Spreading of patients over 3 arms did not reveal major differences in patient characteristics. A very early survival study on 229 patients did not show any statistical difference between the 3 arms.
We hope to present an updated report on time-to-progression and survival.

22

PRELIMINARY RESULTS OF PHASE III STUDY OF MITOMYCIN C VERSUS ESTRAMUSTINE IN PROGRESSIVE METASTATIC PROSTATE CANCER REFRACTORY TO HORMONAL THERAPY - RESULTS OF EORTC GU GROUP STUDY NO.30865

D. Newling, S. Fossa, U. Tunn, K.H. Kurth, M.de Pauw, R.Sylvester and members of the EORTC GU Group

Introduction
A Phase III study of high dose Estramustine phosphate, 540-700 mg a day versus Mitomycin C in 15 mg/m every six weeks has been carried out by the EORTC GU Group.
Patients/Material and Method
All patients had proven progressive metastatic prostate cancer following primary or secondary hormonal therapy. 175 patients with progressive advanced metastatic prostate cancer were prospectively randomized to receive either Mitomcyin C, 15 mg/m every six weeks or Estramustine, 560-700 mg daily.
Results
There was no difference in either arm with regard to survival or time to progression of the patient's prostatic cancer. The median time to progression was 5 months and median survival 10 months in both arms. Both the treatments were associated with significant toxicity.
Discussion
These results suggest that in patients who have relapsed following hormonal therapy and particularly those who have received more than one previous therapy, there is no place for potentially curative therapy with the most active chemotherapeutic agent we have at our disposal, Mitomycin C, or with high dose combination chemotherapy and cytotoxic treatment. At this stage the clinician's aim should be improvement of the patient's quality and not necessarily quantity of life.

23

NEU GENE AMPLIFICATION AND OVEREXPRESSION IN DUCTAL CARCINOMA IN SITU OF THE BREAST.

Marc J. van de Vijver, Johannes L. Peterse, Wolter J. Mooi, Els Wagenaar and Roel Nusse, Dept. of Molecular Biology, Netherlands Cancer Institute, Plesmanlaan 121, 1066 CX Amsterdam, The Netherlands

Neu gene amplification is observed in 10-40 % of invasive breast carcinomas. We have raised 2 monoclonal antibodies reactive with the neu protein and used these antibodies in immunohistochemistry on paraffin sections. In tumors with neu gene amplification a strong membrane staining of tumors cells is present. In tumors with a normal neu gene copy number no specific staining can be detected.
We have analysed various breast lesions for overexpression of neu protein. Neu protein overexpression is present in 14 % of invasive breast tumors. We have not found a strong association with poor prognosis in patients with stage II breast cancer.
Neu protein overexpression is also frequently found in ductal carcinoma in situ (DCIS) of the breast. We have now studied 113 DCIS. 24 out of 25 tumors with a comedo growth pattern; 25 out of 39 with a solid growth pattern; 1 out of 6 with a clinging growth pattern; and 3 out of 43 with a cribriform or papillary growth pattern showed neu overexpression.
We have isolated DNA and RNA from two DCIS showing neu protein overexpression. In both tumors the neu gene was amplified and overexpressed at the RNA level.
We conclude that neu gene amplification, resulting in neu protein overexpression, is an early step in the development of a specific type of DCIS. Neu gene amplification and protein overexpression may result in higher tumor growth rate, but not in increased metastatic potential of breast tumors.

24

THE ANDROGEN RECEPTOR: FUNCTIONAL STRUCTURE AND EXPRESSION IN PROSTATE TUMORS

J. Trapman*, P.W. Faber*, C. Ris-Stalpers**, C. van Laar**, K. Ruizeveld de Winter*, N. Zegers****, F.H. Schröder***, Th.H. van der Kwast*, E. Mulder** and A.O. Brinkmann**
*Dept. of Pathology, **Dept. of Biochemistry II, ***Dept. of Urology, Erasmus University, Rotterdam, and ****Lab. Immunology, MBL/TNO, Rijswijk, The Netherlands.

The androgen receptor is a nuclear protein which plays a key role in development and functioning of the prostate gland. The growth of the majority of prostate tumors can be inhibited by blockade of androgen receptor action. However, this inhibition is transient. Detailed knowledge of androgen receptor function and synthesis will contribute to our understanding of the processes described above. The molecular cloning of androgen receptor cDNA and the generation of specific antibodies against the receptor provide the tools for the study of these processes. Results obtained so far provide evidence that: 1. Androgen receptor mRNA expression is androgen-dependent. 2. Androgen receptor mRNA expression is low or absent in androgen-independent prostate tumor cell lines. 3. Androgen receptor expression is in general lower in less-differentiated prostate tumors than in well-differentiated tumors. 4. The androgen receptor of the LNCaP prostate cancer cell line is mutated.