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11.019

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MONOCLONAL IRMA OF SERUM TPS IN PATIENTS WITH GYNAECOLOGIC CANCER : COMPARISON WITH TPA AND 5 TUMOUR MARKERS

After TPS, an epitope of tissue polypeptide antigen (TPA), had been recognized as a proliferation marker, it was of interest to investigate the serum concentration of TPS in patients with malignant gynaecologic tumours.
In 42 serum samples taken from 21 women (13 with breast carcinoma, 4 each with malignant ovarian tumour or uterine carcinoma of different stages) TPS, TPA, CA 15-3, CA 125, CA 72-4, CA 19-9 and CEA were determined. A monoclonal immunoradiometric assay (IRMA) was used.
Serum TPS was raised in 5 patients (3 with breast carcinoma, one each with malignant ovarian tumour or uterine carcinoma), serum TPA in 19 patients (12 with breast carcinoma, 4 with malignant ovarian tumour, 3 with uterine carcinoma). Serum CA 15-3 was elevated in 14, CA 125 and CA 72-4 each in 9, CA 19-9 and CEA each in 5 women.
In conclusion, serum TPS proved to be a proliferation marker the rise of which mainly appeared to reflect an increase of the proliferation rate or growth activity of tumour cells.

11.020

Suramin and Doxorubicin: additive antitumorigenic effect evaluation on mammary carcinoma cell lines (HBCCL).

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Suramin (Sur), a polysulfonic drug, has been demonstrated to have cytostatic reversible activity on ER+ and ER- HBCCLs. Doxorubicin (Dx) is still the most active agent presently available for the treatment of advanced breast cancer. In order to evaluate a possible additive or synergic inhibitory effect on the proliferation of ER+ MCF-7 and the estrogen independent LCC1 HBCCLs we have investigated, by the colorimetric MTT assay (J. Carmichael, C.Res.47,'87), the effect of Dx and Sur alone and in sequential combination. Over a period of 4 days of culture, the administration of Dx (0.4 µg/ml, 2 h) showed an inhibitory effect of 44% and 17% on MCF-7 and LCC1 respectively, while Sur (200 µg/ml, 96h) inhibited the growth of MCF-7 of 50% and LCC1 of 39%. The administration of Dx (2h) followed by Sur (94 h) caused an inhibition of 60% on MCF-7 and 53% on LCC1 cell lines. We report here that the sequential exposure of cells to both molecules enhances the inhibitory effect of the single administration, suggesting that it could be possible to obtain the same cytotoxic effect at lower doses of drugs.

11.021

A FOUR DRUG COMBINATION CONTAINING VEPESID IN THE TREATMENT OF SMALL CELL LUNG CANCER(SCLC)

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A phase III clinical study in SCLC was made, using a original combination consisting of :

VEPESID - 80 mg/m^2 on d. 1 to 5
Vincristine - 1,2 mg/m^2 on d. 1 + 8
Methotrexate - 30 mg/m^2 on d. 1 + 8
Cyclophosphamide - 300 mg/m^2 on d. 1 + 8

On the study entered 34 patients with SCLC, 33 male, mean age 57y, performance status - media 80. The responce rate (at least after 2nd course) is : CR in 8,8 %; PR - 23,6 % and stable disease in 55,6 %. The obtained objective responce of 32,4 % as a preliminary result is good. The proposed combination is an effective one and the study goes on with the final aim to evaluate the survival rate.

11.022

A PHASE II OPEN STUDY OF ZOFRAN IN PLATINUM CONTAINING REGIMENTS

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An open phase II clinical study of ZOFRAN was conducted in 18 patients who underwent a combination chemotherapy containing a single application of Platinum at a dose of 80mg/m^2. It was used a modifide scheme of treatment with ZOFRAN : 8 mg amp. before Platinum, 8 mg amp. 4 hours later and after that the treatment continue with tablets - 8 mg at 8 hour intervals, up to 3 tabl. for a course. In all the patients the vomiting was not observed and nausea was reported in one patient (mild). No side effects were registered. The authers propose this way of application of ZOFRAN in a moderate doses as a effective, improving the quality of life in cancer patient on chemotherapy regiments containing Platinum.

11.023

INHIBITION OF THE GROWTH OF ADENOCARCINOMA IN AN ANIMAL MODEL OF LIVER METASTASES BY OCTREOTIDE.

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The treatment of metastatic liver cancer remains poor, the majority of patients dying within one year of diagnosis. Adenocarcinoma is the commonest cancer metastatic to the liver. Octreotide, a long acting analogue of somatostatin alters liver blood flow, stimulates reticuloendothelial system activity and inhibits a wide variety of trophic hormones. We have investigated its effects on the growth and development of hepatic adenocarcinoma induced by intra portal inoculation of tumour cells. Following intraportal injection of 1 x10^7 K12\Tr cells, (an adenocarcinoma of colonic origin syngeneic to the BDIX rat), groups of 12 rats received either Octreotide 2 ug bd or saline (control). At 4 weeks there was a significant reduction (Mann Whitney U, P<0.001) in the number of tumour nodules in the treated group; [median 3 (range 7-0) compared to controls median 21 (range 33-24)]. Furthermore no tumour was present in 4 of 12 livers in the treatment group. These results indicate that Octreotide significantly inhibits growth and development of hepatic adenocarcinoma of colonic origin in the rat and may be of benefit in the treatment of hepatic metastases in man. Further studies are required to evaluate this hypothesis.

11.024

EFFECTS OF ANTHRACENE-9,10-DIONES ON DNA TOPOISOMERASE II-MEDIATED DNA CLEAVAGE

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Mitoxantrone (MIT), a potent cytotoxic drug is a intercalator that induces topoisomerase II-mediated DNA cleavage. MIT and one analogue with a modified side chain (BBR2577) were compared for their cellular effects and interference on enzyme activity. Cytotoxicity studies on a human small cell lung carcinoma cell line showed that BBR2577 was 3-times more potent than MIT. Drug uptake was similar. Cell DNA breaks induced by the two drugs were comparable and dose dependent up to 1 µM. The quantitative relation between cytotoxicity and DNA cleavage indicated a behaviour more similar to that of epipodophyllotoxins than that of doxorubicin. Cleavage of SV40 DNA with the purified topoisomerase II showed an identical DNA cleavage pattern though BBR2577 was 2-fold more active than MIT. The correlation between enzyme-mediated DNA cleavage and cytotoxic action of anthracene-9,10-diones supports a critical role of drug interference with topoisomerase II function.