

Thrombocytopenia G1-2 in 4, mild nausea-vomiting in 12 and weight gain in 5 patients.

**Conclusion:** The combination of carboplatin, methotrexate, 5FU and MPA is highly active with acceptable toxicity in pts with advanced endometrial cancer.

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PUBLICATION

### Koilocytotic lesions and cervical cancer in Moldova: An morphoepidemiological study

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**Purpose:** Recent data suggest that there may be geographical or ethnic differences in the prevalence of genital HPV infection, HPV-related benign and neoplastic lesions. The medical assistance to patients with cancer is assured in Moldova by the Oncological Institute. In 1996 our institute receives from the whole republic 273 patients with invasive cervical carcinoma. Surprisingly, only 274 cases of koilocytosis present within exocervical epithelium were recorded in this year.

**Methods:** Biopsy specimens from 274 women with cervical abnormalities were examined in order to analyse the link between koilocytosis – the morphological evidence of HPV-infection, and cervical cancer precursors. Ultrastructural (TEM) examination of 42 different koilocytotic lesions was performed to determine virus particles and cellular alterations associated with koilocytosis.

**Results:** Koilocytes were found in biopsies from 182 women (median age, 33 years) with low-grade CIN, 64 patients (m. age, 39 years) with high-grade CIN and 28 patients (m. age, 46 years) with microinvasive carcinoma, in proximity to cancerous lesions. HPV-like particles (45–50 nm in diameter) were found in koilocytes in 6 out of 42 cases studied by TEM. No virus particles were observed in neoplastic cells.

**Conclusion:** It is likely that there is temporal and spatial relationship between koilocytotic lesions and cervical carcinomas. However, only a small percentage of carcinomas can be related to HPV infection by means of the routine histopathological methods.

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PUBLICATION

### Neoadjuvant chemotherapy followed by radical hysterectomy or radiotherapy for FIGO III and IV cervical cancer: A pilot study

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#### Objective:

- (1) Neoadjuvant chemotherapy – a possible alternative to primary conventional radiotherapy?
- (2) How does it improve overall-survival and quality of life?

**Patients and Methods:** Between February 1991 and February 1993 25 patients with locally advanced squamous cell carcinoma of the cervix (22 stage III B and 3 stage IV A) were enrolled in this pilot study. All of them were treated with Cisplatin 30 mg/m<sup>2</sup> and 5-Fluorouracil 1 g/m<sup>2</sup>, administered intravenously on three consecutive days. This regimen was repeated after four weeks. After the second course the response was evaluated. A third course was given to patients with partial or complete response followed by radical hysterectomy and pelvic lymphadenectomy. The other patients received radiotherapy.

**Results:** The chemotherapy regimen was well tolerated and followed by a 72% overall remission rate. All these 18 women underwent radical hysterectomy. Today after a median follow up of 57 month 10 (56%) of the patients with hysterectomy are alive and free of disease, 5 (28%) have died because of cancer and 2 (16%) are alive and, however, show recurrence. The 7 (28%) patients with disease progression under chemotherapy were treated with standard teletherapy and brachytherapy. 6 patients in this group died because of cancer, and one is still alive and free of disease.

**Conclusion:** The neoadjuvant chemotherapy followed by radical hysterectomy and pelvic lymphadenectomy in this pilot study seems to be an alternative method for treatment of advanced cervical cancer with excellent response rate and acceptable compliance.

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PUBLICATION

### Gynaecological cancer: Advantages and possibilities of intraarterial polychemotherapy

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**Purpose:** In gynaecological cancer patients the improving of the results of the treatment, the raising operability by using intraarterial polychemotherapy (IAPCT) was evaluated.

**Methods:** Superselective intraarterial polychemotherapy as a stage of the combined or complex treatment has been used in 152 patients with malignant tumors of female genitals: 15 patients with uterine corpus cancer (UCC), in 78 cervical cancer patients (CC), 41 – with trophoblastic tumors (TT), 18 – with disseminated ovarian cancer (DOC).

**Results:** One or two courses of superselective IAPCT each consisted of 3–4 seances of prolonged infusion of cytostatics (platinium, methotrexate, endoxan, bleomycin, 5-fluorouracil) have been used. To confirm the effectivity of IAPCT pathomorphosis of female genital tumors have been studied. The obtained morphometric results testify to the fact that in UCC patients necrosis of tumorous tissue took place in 46.5%, in CC – in 67.8%, in TT – 87.3%, in DOC – in 31.4%. Remission lasted for 12 months in 86.24 ± 5.26% patients with CC without regional metastases (N-0), 24 months – 80.49 ± 6.28%; 36 months – 75.12 ± 7.83%. In (N-1) – 84.22 ± 4.70%; 76.34 ± 5.14% and 70.18 ± 6.75%, respectively. Survival of cervical cancer patients was in N-0 and in N-1-12 months – 97.85 ± 2.13% and 96.8 ± 2.43%, respectively; 24 months – 94.69 ± 3.73% and 90.2 ± 4.87%, respectively.

**Conclusion:** IAPCT in complex therapy of malignant genital tumors gives an opportunity to raise operability of UCC and CC and in TT – in the majority of cases – to escape surgical intervention. Remission duration in DOC and the results of treatment did not differ from that in intravenous polychemotherapy. Preoperative IAPCT in patients with UCC and CC improves both immediate and remote results of the treatment, promotes extension of the operability of locally advanced forms of cervical cancer.

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PUBLICATION

### Tamoxifen and vaginal and cervical cytology and sonographical changes of endometrium

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**Purpose:** Tamoxifen is an essential part of adjuvant endocrine therapy of breast cancer. We examined the effect of tamoxifen on proliferation of vaginal epithelium and cervical glands.

**Methods:** Determining the changes of endometrium and uterus by ultrasound we tried to find correlations to cytological results. 90 patients with breast cancer coming in our oncological outpatient clinic were treated with tamoxifen. We determined the thickness of the endometrium by ultrasound and measured the uterus. At the same time we took a vaginal and cervical brush in order to find out the maturation index of vaginal epithelium and hyperplasia of endocervical cells.

**Results:** The maturation index of vaginal epithelium was in the range of 0.55–0.75. We found in 50% a sonographically suspect endometrium. In about 66% percent we found hyperplasia of endocervical cells.

**Conclusions:** Tamoxifen has a proliferative effect on vaginal epithelium and endocervical cells. Simultaneously sonographical changes of endometrium can be found.

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PUBLICATION

### Cervical cancer screening: Results of two years of a French pilot study in 3 districts of Lyon suburbs

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**Aims:** Increase attendance rate to a CCS, especially for high risk group, helped by intensive collaboration of local practitioners and social workers.

**Methodology:** Since november 1993, a cervical cancer screening program has been initiated in 3 districts of Lyon suburbs. A free cervical smear (CS) was proposed to 30.846 women, from 25 to 65 year-old, living in one of the three target districts. Women information was performed by sending a personalized letter and using local audio visual possibilities. During medical consultation, epidemiologic informations were collected for each woman,

about her previous gynaecological screening. During the two studied years, 3699 women were included, i.e. a crude participation rate of 12%, hardly increased for women over 60. A strong decrease of participation has been noted after the 6th month of the campaign. In this series, 60.5% of women had an insufficient screening, without relation on age. Only 1.8% of CS were uninterpretable and only 1.9% of them were pathologic.

**Conclusion:** Despite original information, low crude attendance rate was noted, but high rate of insufficient prevalent gynaecological follow-up may be underlined

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## PUBLICATION

### Concomitant radiochemotherapy with or without surgery in poor pronostic cervical cancer: A pilot study

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**Purpose:** To evaluate the role of concomitant radiochemotherapy (CRC) in the treatment of poor pronostic cervical cancer, we reported the results of 38 patients (pts) in term of locoregional control, toxicity and survival.

**Methods:** we have treated from february 1990 to october 1995, 38 pts using six courses of 5 FU (500 mg/m<sup>2</sup>/d) and cisplatin (20 mg/m<sup>2</sup>/d) in continuous infusion for 5 days, every 3 weeks. A split course radiotherapy (15 Gy in twice daily fractions of 1.5 Gy for 5 days) was delivered concomitantly with the first 4 chemotherapy cycles. A Wertheim procedure was made before CRC in the group A (12 pts), after 2 CRC cycles in group B (10/13 pts) and not in group C (13 pts).

**Results:** the median follow-up was 27 months. We have obtained in 25 evaluable patients 72% objective response (10 complete response and 8 partial response). In the group C, the CR was 61%. The hematological toxicity was acceptable (18% grade OMS III-IV). A neurotoxicity G II was occurred in 7 pts (18%) and renal toxicity G II in one pt. In the group A, 2 had a second surgery for bowel obstruction. A locoregional recurrence was observed in 18 pts (47%). The disease-free survival at 3 years was 62%. The actuarial overall survival at 3 years was 73% (75% group A, 100% group B and 44% group C with a median survival of 32 months). 8 pts died, 2 of local disease, 5 of local and métastatic disease and 1 of toxic complication.

**Conclusion:** this CRC with or without surgery obtains a good result in term of the locoregional control. The toxicity was acceptable excepted the neurotoxicity in group C. The disease-free survival and overall survival are satisfactory specially in group A and B.

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## PUBLICATION

### Plasma kallikrein-kinin system in patients with tumors of reproductive system operated and submitted to radiotherapy

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A complex evaluation of kallikrein-kinin system and selected parameters of proteolytic-antypoteolytic system in plasma 21 women operated on because of uterine or endometrial carcinoma and submitted to radiotherapy. Samples of blood were collected before and after irradiation.

The patients (in comparison to control) both before and after radiotherapy demonstrated an increase of prokallikrein concentration (biological and chromogenic method), a decrease of low molecular weight kininogen concentration and a decrease of kininase activity (biological method), an increase of antipapain activity dependent on kininogen (caseinolytic method), a decrease in fibrinogen concentration (tyrosin method), and an increase of protein as inhibitor antigens (immunodiffusion methods).

The irradiation induced a significant decrease in concentration of low molecular weight kininogen, protein fibrinogen and antigen C<sub>1</sub>INH. Besides the increase of antigens AT III and α<sub>2</sub> M. a decreasing tendency in other parameters values were observed.

It may be concluded that in the investigated patients the components of plasma kininogenesis, including bradykinin, enhance antiproteolytic and antithrombotic barrier of plasma.

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## PUBLICATION

### A phase II trial of methotrexate, vinblastine, doxorubicin, and cisplatin (MVAC) in metastatic cancer of the uterine cervix

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**Purpose:** Patients with metastatic cancer of the uterine cervix have a limited survival. Thus, new chemotherapeutic agents and combinations are needed to improve patients outcome.

**Methods:** Twenty-seven patients with stage IV primary or recurrent cervical cancer were assigned to chemotherapy with MVAC consisting of methotrexate 30 mg/m<sup>2</sup> iv on days 1, 15 and 22, vinblastine 3 mg/m<sup>2</sup> iv on days 2, 15 and 22, doxorubicin 30 mg/m<sup>2</sup> iv on day 2, and cisplatin 70 mg/m<sup>2</sup> iv on day 2. Granulocyte colony-stimulating factor (G-CSF) was given subcutaneously on days 6 to 10 at a dose of 5 µg/kg. The treatment was given on an outpatient basis and courses were repeated every 4 weeks for a maximum of 6 cycles.

**Results:** After a median of four cycles, we observed objective responses in 14 patients (52%), including three complete responses (11%), and eleven partial responses (41%). Median overall survival was 11 months (range, 4 to 18+), and median progression-free survival of the responding patients was 8 months (range 6 to 18+). Grade 3 or 4 toxicities (WHO): neutropenia 45%, thrombocytopenia 19%, anemia 15%, Mucositis 22%. There were no treatment related deaths.

**Conclusion:** MVAC is an active regimen in patients with advanced or recurrent cervical cancer. It produces responses in one-half of them, and can be safely administered on an outpatient basis.

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## PUBLICATION

### Detection and typing of human papillomavirus type 6/11, 16 and 18 infection in squamous cell carcinoma of uterine cervix in Taiwan

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**Purpose:** Ample evidence has shown that HPVs are etiological agents of human cervical cancer. In this study, thirty biopsied specimens of invasive squamous cell carcinoma of the uterine cervix were examined for the presence of human papillomavirus (HPV) DNA.

**Method:** We used three types of HPV probes (HPV-6/11, 16 and 18) to detect the prevalence of HPV infections by less stringent dot blot hybridization. HPV DNA could be found in 25 (83%) of 30 cases. The typing of HPV was performed by both above methods under highly stringent conditions.

**Results:** There are 8 cases with HPV-16 infection, 2 cases with HPV-6/11 infection and one case contained HPV-6/11, 16 mixed infections. There was no HPV-18 infection in our studies.

**Conclusion:** Less stringent conditions allowed hybridization of weakly homologous regions and so permit detection of multiple HPV types with any one HPV probe. They are employed for screening specimens. Stringent conditions were employed for detection of specific HPV types.

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## PUBLICATION

### Therapeutic approach in stage III of cervix carcinoma

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Currently, radiotherapy (RT) associated with chemotherapy is considered to be the main therapeutic attitude and according to some authors the only one in stage III B of cervix carcinoma.

The aim of this study is to define the place of surgery in the therapeutic approach of stage III B cervix carcinoma.

This paper evaluates 5 years survival related to the treatment on 147 patients with stage III B cervix carcinoma treated between 1990-1991 in the Institute of Oncology Bucharest.

Treatment was initiated with RT (external irradiation delivering on average 50 Gy to the pelvis followed by intracavitary irradiation up to 30 Gy). Based on good response to RT, in 79 selected patients the treatment was followed by surgery with curative intention. Only in 49 cases radical colpohysterectomy with pelvic lymphadenectomy was possible.

Overall survival was 40.13% at 3 years and 30.61% at 5 years. 5 years survival relates to the therapeutic approach (36.71% for those patients