THE EXTRACORPOREAL IMMUNOPHARMACOTHERAPY (EIPHT) AND REMOTE RESULTS OF CERVICAL CANCER AND OVARIAN CANCER TREATMENT

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Introduction The aim of this study was to investigate the effect of extracorporeal immunopharmacotherapy on long-term results of treatment of cervical cancer and ovarian cancer.

Material and methods The study included patients with cervical cancer and ovarian cancer T2-3N0-1M0 stages, w All the patients with ovarian cancer in a combined therapy of adjuvant or neoadjuvant mode comprising combination chemotherapy of cisplatin 75mg/m²+Cyclophosphan 1000mg/m² for 4 days at 4–6 courses 1 every 3 weeks and surgical treatment within the scope of radical surgery. EIPHT was performed by exfusion of 500–1000 ml of autoblood in 'Gemakon' or 'Terumo' sterile containers and its centrifugation at 3000 rpm for 30 min. Then the obtained leukotrombomass and erythrocytic mass were incubated with thymalin in a total dose of 30 mg (for 3 procedures) at 37º C for 60–100 min, with the subsequent return of the conjugate to the circulatory system of patients. In total, patients received 2 sessions of extracorporeal therapy at the beginning of admission to hospital and before discharge from the hospital.

Results and discussions Depending on the type of EIPHT being performed, 4 groups of patients with cervical cancer and OC were isolated. The 1st group (34 patients) included patients with cervical cancer and OC who did not receive immunotherapy. In 2nd (32 patients) cervical cancer and 42 patients with OC, immunotherapy in the form of subcutaneous injections of thymomimetics (thymalin) in standard doses for 4 days at 3–4 courses 1 every 3 weeks and surgical treatment within the scope of radical surgery. EIPHT was performed by exfusion of 500–1000 ml of autoblood in 'Gemakon' or 'Terumo' sterile containers and its centrifugation at 3000 rpm for 30 min. Then the obtained leukotrombomass and erythrocytic mass were incubated with thymalin in a total dose of 30 mg (for 3 procedures) at 37º C for 60–100 min, with the subsequent return of the conjugate to the circulatory system of patients. In total, patients received 2 sessions of extracorporeal therapy at the beginning of admission to hospital and before discharge from the hospital.

Conclusion The use of EIPHT methods in the complex therapy of oncogynecologic diseases makes it possible to increase the parameters of the five-year total and disease-free survival of patients with cervical cancer and ovarian cancer.

THE IMMUNOREACTIVITY OF PATIENTS WITH CERVICAL CANCER ON THE BACKGROUND OF EXTRACORPOREAL IMMUNOPHARMACOTHERAPY (EIPHT)

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Introduction The aim of the study was to study the state of cellular and humoral factors of immunity of cervical cancer patients on the background of using extracorporeal immunopharmacotherapy.

Material and methods 136 patients with cervical cancer T2-3N0-1M0 stages. With cervical cancer IIA, the stage of the disease was observed in 18.7% of cases, IIB - in 20.9%, IIIA - in 16.0% and IIIB stage - in 44.4% of cases. The largest part of the patients was female cervical cancer at stage IIIB. Depending on the methods of therapy in the complex treatment: group 1–36 patients with cervical cancer before treatment; 46 patients with cervical cancer who received EIPHT with thymalin; group 3–54 patients with cervical cancer who did not receive EIPHT. Also 34 persons of the control group with normative values. The study of the immune system was carried out at the admission of patients to the hospital before the immunotherapy course and immediately a few days before discharge from the hospital. All patients with cervical cancer received standard polychemotherapy according to the protocol of the department, a complex treatment including a two-stage combined radiation therapy. Immunological studies included the study of cellular and humoral parameters of the immune system of patients with cervical cancer. The EIPHT method was designed primarily to reduce toxic effects after chemotherapy and radiotherapy, as well as improve the overall condition after chemotherapy and radiation therapy.

Results and discussions The analysis showed that patients with cervical cancer was found a T-cell immunodeficiency, which was associated with CD4+ - deficiency against the background of an increase in CD8 + and increased activation of lymphocytes with the predominance of apoptosis of immunocompetent cells. After carrying out EIPHT with thymalin, activation of the T-cell link of immunity is observed. The revealed imbalance of the humoral link of immunity before and after polychemotherapy and radiotherapy was associated with an imbalance of the main serum immunoglobulins and an elevated CIC level of small and large values. Against the background of the use of EIPHT with thymalin, normalisation of humoral factors of immunity and activation markers of lymphocytes is observed.

Conclusion Thus, the method of EIPHT in our case turned out to be promising in the treatment of cervical cancer due to the possibility of removing the effects of cancer and chemoradiation intoxication, as well as activating its own system of antitumor protection of the organism.
Material and methods We have designed an interventional project included in the HoTBreast trial: the extended use of HT as an NA for breast cancer patients who refuse surgery or are considered inadequate to receive it, in the context of close surveillance. In this group of extended NA treatment patients, different hormone treatment strategies (aromatase inhibitor and tamoxifen) are allowed to be used, depending on tumour response and patient quality of life. During treatment, clinical and imaging (ultrasound) follow-up will be implemented every two to three months in the first 3 years and every four to six months after that. The treatment option can be changed at any time if considered appropriate, based on disease response or progression and the patient’s quality of life. This group will be randomly divided into two subgroups, one who will receive hormone treatment alone and a second one who will receive HT and aspirin. Aspirin plays the role of an anti-inflammatory controller and it is not clear what the relation between chronic inflammation processes and breast cancer is – this is a new approach for cancer treatment with a strategy targeting the tumour microenvironment. Our secondary objective is to understand if the local disease presents the same response as the systemic one (in cases where this also exists) or if it can be used as an independent predictor of disease behaviour.

Results and discussions We believe that HoTBreast trial can give some answers about the best practice for treating early BC. We also expect that it can shed some light on the question of the role of surgery in early BC and the use of aspirin in BC patients. We acknowledge the hypothesis that aspirin can improve the treatment of BC patients in a safe, well tolerated and inexpensive way.

Conclusion Efforts should be made to better communicate to patients that NA HT is a valid option and sometimes the most appropriate for the specific patient. The decision should depend on the patient, based on an informed understanding of the benefits and risks of avoiding surgery.

PO-259 IDENTIFICATION OF A CLINICALLY MEANINGFUL SITE-SPECIFIC STEROID ROADMAP IN PROSTATE CANCER.

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Introduction In prostate cancer the genotype of the tumour does not always predict clinical behaviour and disease aggressiveness after castration therapy. Additional factors might be important. Here we hypothesise that there is a site-specific steroid profile roadmap after castration that is of clinical significance.

Material and methods Steroid profiles in blood plasma (BP) and bone marrow aspirate plasma (BMA) from 120 castrated patients with prostate cancer were evaluated with mass spectrometry. We studied the steroid ligand-receptor interactions in prostate cancer adrenal metastases (PCAM) because they represent a steroid-rich environment. Adrenalectomy specimens from 3 castrated patients with PCAM were analysed.

Results and discussions It is known that normally BP/Adrenal vein plasma testosterone (T) concentration ratio is approximately 1:1 and cortisol (C) ratio is roughly 1:3. We measured similar T levels in BP and BMA. The levels of C were significantly lower in BMA compared to BP. Our data suggest that T levels are uniform but there is a C concentration gradient between the different compartments. Cortisol acts through GR and in the presence of T is a partial AR inhibitor.

All PCAM samples had functional androgen receptor (AR) (wild-type (wt), no copy number changes) and glucocorticoid (GR), but no progesterone receptor (PR). No DHT was detected. Patient 1 tumour was able to synthesise T and had above castrate intra-tumoral T levels. The tumour lacked enzymes to synthesise, but was able to catabolize C. The levels of C were within the normal BP range. Gene expression of AR was normal. Patient 2 and 3 samples had castrate T and high C levels (3-fold BP), but AR gene expression was remarkably high. All patients had PTEN and RB deletions, while patients 2 and 3 had mutant (m) p53.

Addition of 40 ng/dl T increased growth in vitro in a xenograft PCAM model (propagated in matrigel) derived from patient 1. When C was concomitantly added at high levels such as those in patients 2 and 3, PCAM growth returned to baseline (no steroids), suggesting that almost all T or C activity were lost. Moreover, proliferation in VCAP cells (High AR/GR+) decreased when high C was added in low T, but remained well above baseline, generating the hypothesis that this steroid combination mostly inhibits AR/GR tumours with non-amplified AR (e.g. early in castration).

Conclusion There is a clinically meaningful site-specific steroid roadmap. The PCAM steroid profile may serve as a useful model to elucidate tumour interactions with the steroid environment.

PO-260 DEEP PHENOTYPING OF COLORECTAL CANCERS BY HIGH-DIMENSIONAL MASS CYTOMETRY REVEALS TUMOR-SPECIFIC IMMUNE LANDSCAPES

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Introduction Immune checkpoint blockade has revolutionised cancer treatment. However, clinical outcomes are highly variable as only a proportion of cancer patients benefit from this treatment. To understand the mechanisms that determine responses to current immunotherapies and for the design of alternative approaches, it is crucial to characterise the immune landscape of the tumour microenvironment. An in-depth understanding of anti-tumour immunity requires a comprehensive analysis of the immune cell populations that participate in the process of tumorigenesis. The aim of this study is to unravel local and systemic profiles of lymphoid and myeloid immune subsets in colorectal cancer (CRC) using high-dimensional immunophenotyping by mass cytometry.

Material and methods The expression of 36 immune cell markers was simultaneously assessed at the single-cell level by mass cytometry in tumour tissues (n=19), tumour-associated lymph nodes (n=17), adjacent normal mucosa (n=4), and peripheral blood samples (n=9) derived from 18 CRC patients. In total, 9 million cells were included in the analysis. Cytospore and HSNE (Hierarchical Stochastic Neighbour