Welcome to CRCT 2023

It is with great pleasure that we welcome you to the beautiful city of Dubai for the International Conference on Cancer Research and Clinical Trials (CRCT-2023), in Dubai on March 16, 2023.

First, we would like to thank all of you for your participation at the conference. We are aware that many of you have had difficulties obtaining funding, visas, and travel tickets, and many have travelled a long way to reach us. Thank you!

Clinical trials are the final step in a long process that begins with research in a lab. Clinical trials for cancer are research studies that compare the most effective known treatment for a specific type or stage of cancer with a new approach. This conference will be a platform for the members to explore current and future research directions, innovative treatments, discuss about leading-edge research and clinical trials, the next generation treatments, new ways to prevent and detect cancer and latest therapies to improve cancer care for fu-ture patients. It is a pleasure for us to offer you the abstract book for CRCT 2023.

All accepted abstracts for the International Conference on Cancer Research and Clinical Trials (CRCT-2023) will be published in the Conference Proceedings as well as in the Brit-ish Journal of Cancer Research (Online ISSN-2631-5297) with a permanent DOI number.

Our warmest thanks go to all invited speakers, delegates, and contributors to CRCT 2023 for accepting our invitation, visiting Dubai, and using CRCT 2023 as a medium for com-municating your research results. We hope that you will enjoy the conference and look forward to meeting you again at one of the forthcom-ing CRCT 2024 events.

We do hope that you enjoy your attendance at CRCT 2023!

SCIENTIFIC COMMITTEE

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Cardiotoxic Effects of Antitumor Agents: Pathogenetic Mechanisms

Alexandros Tselepis, MD, PhD

Professor, Biochemistry-Clinical Chemistry Atherothrombosis Research Centre, Department of Chemistry, University of Ioannina, 45110 Ioannina, Greece, Tel: +30 26510 08365; Fax:+30 26510 08677

Abstract

Cancer treatment is associated with various side effects of antitumor agents, which increase the morbidity and mortality of these patients. Cardiotoxicity is perhaps the most serious non-haematological side effect of the anticancer drugs. The antitumor drugs that express cardiotoxic effects include anthracyclines, tyrosine kinase inhibitors, taxanes, fluoropyrimidines, alkylating agents, vascular endothelial growth factor inhibitors, immune checkpoint inhibitors, proteasome inhibitors and human epidermal growth receptor type 2 antibodies. The spectrum of cardiotoxic effects of anticancer drugs is broad and include, among others, heart failure, arrhythmias such as atrial fibrillation and ventricular tachyarrhythmias, hypertension (systemic or pulmonary), cardiomyopathy, myocarditis, valve disease, pericardial disease, vascular events (arterial thrombosis, venous thromboembolism) and myocardial ischemia (acute coronary syndrome, angina). The molecular mechanisms by which anti-cancer therapies lead to cardiotoxicity are diverse and vary according to the specific type of agent used. They include oxidative stress, topoisomerase 2-β inhibition in cardiomyocytes, inflammation, endothelial dysfunction, apoptosis, disruption of Ca^{2+} homeostasis, mitochondrial dysfunction, DNA damage, increase in various circulating microRNAs levels, alterations in the function of voltage-gated potassium channels. The management of cardiovascular complications in cancer patients is a new challenge for oncologists and cardiologists. Thus the cardio-oncology field has developed the last decade in order to precisely predict and efficiently treat the cancer treatment-related cardiovascular diseases.

Biography

Alexandros Tselepis has graduated in Pharmacy (University of Thessaloniki) and in Medicine (University of Ioannina, Greece). He obtained his PhD in Clinical Biochemistry at the University of Ioannina. His research work continued with a postdoctoral fellowship (Fogarty, NIH) in the Pathology Department, University of Texas Health Science Centre, at San Antonio, USA (1988-89). From 1994 to 1999 he took a sabbatical leave and conducted research work on lipoproteins and atherosclerosis as an invited researcher in INSERM U321 Paris, France. Currently he is the Professor of Clinical Biochemistry, Director of the Atherothrombosis Research Centre (http://atherothrombosis.lab.uoi.gr) and President of the interdepartmental Postgraduate Programme “Medical Chemistry” of the University of Ioannina (http://medchem.ac.uoi.gr). His main research interests concern the pathophysiology of Atherothrombosis. He has supervised 25 PhDs, 35 MSc and 10 postdocs and he has an over than 25 years’ experience in managing international and national research projects. Currently he has 272 publications in peer reviewed journals and more than 10,000 citations, whereas his h-index is 47, according to scopus.

Multicentral Preventive Antibiotics with Cystectomy within Enhanced Recovery after Surgery (MACS trial): Initiating of the Study

Belyaev A. M., Nosov A. K., Mamizhev E. M., Shchekuteev N. A., Rumyantseva D.I., Berkut M.V

FSBI "N. N. Petrov NMRC of oncology" MH of Russian Federation, St. Petersburg, Russia

Abstract

Radical cystectomy (RC) with uroderivation is a standard surgical operation for muscle invasive bladder cancer (MIBC) and it is associated with a high level of infection complications (up to 40-60%). The option for resolving such complications might be antibiotic prophylaxis (AP). However, the lack of strong evidence to support variations/ combination antibiotics, rapidly changing perioperative prophylaxis paradigms, absent of data for older patient with MIBC (>65 years-old) warrant a randomized clinical trial, especially within combination RC and ERAS protocol. Background/Problem (zero-hypothesis): The use of prolonged AP, calculated depending on the GFR, does not influence on the incidence postoperative infection complications.

Objectives: present short-term interim results (3 months) after study initiation.

Methodology: MACS trial is a first prospective, randomized, multicenter phase 3 study in Russia. ClinicalTrials. gov Identifier is NCT05392634 for detailing inclusion/exclusion criteria. The statistical sample was calculated using "Sample Size Calculators UCSF CTSI, Kohn MA, Senyak J." for reducing the risk of infection complications in group A (standart AP) RR=0.63 to RR=0.32 in group B (prolonged AP). The number of patients required for inclusion in the study is 92 (+ 10% included with the dropout). It was selected 2 criteria for patients' stratification: neoadjuvant therapy (NT) and uroderivation option (ortotopic or heterotopic). Type I error is 5%, type II error is 20%.

Results: Interim analysis was performed for the period 30-05-2022 to 30-08-2022: it was included 17 patients (18.5% of the intended sample size) who underwent RC. Trial was included 16 men (94.1%) and 1 woman (5.9%). The mediana of age was 65.82±6.99 years (54-82 years). The average BMI was 25.21±3.17. NT was carried out in 9 patients (52.9%): chemotherapy 7 cases, immunotherapy 2 cases. Orthotopic uroderivation was performed in 3/17 patients; in other cases Bricker-uroderivation was performed. The median length of hospitalization was 11.13 ±2.17 days. It was revealed 30-day complications as follows: Clavien 3b in 2 cases (migration of ureteral stents 1 case, parastomy incarcerated hernia 1 case), Clavien 2 in the form of asymptomatic bacteriuria according to the results intraoperative seeding in 4/10 cases, Clavien 3a in 1/10 cases (percutaneous nephrostomy for partial J-pouch failure). The series of inflammatory factors have also been identified derived from peripheral blood test results (before surgery and before discharge): differences between groups in neutrophil to lymphocyte ratio (NLR) was not obtained, derived neutrophil to lymphocyte ratio (dNLR) was not obtained, however, in the group of prolonged AP the systemic immune-inflammation index (SII) remained the same high at discharge (decrease from 1130.65 to 550.4 in group A ; in group B from 1114.15 to 1070.54), which may be associated with the activity of the immune system and requires study. Policy

Implications/Conclusions: The interim analysis showed acceptable results in terms of the frequency of infectious complications, none of cases 5th degree of complication detected. The MACS study continues to recruit patients until February 2023.

Table 1. Baseline characteristics.

	Features	Group A		Group B	
		cTNM	pTNM	cTNM	pTNM
TNM (AJCC 8th)	T0	-	0	-	3
	Tis	1	0	0	2
	T1	0	3	2	1
	T2	2	1	4	0
	T3	3	1	1	0
	T4	1	2	0	1
	No	7	4	5	5
	N1-2	0	3	2	2
	Mo	7	7	6	6
	M1	0	0	1	1
Neoadjuvant treatment	No	4		3	
	Yes	3		4	
	GP	2		3	
	MVAC	1		0	
	Immunotherapy	1		1	
Uroderivation	Heterotopic (Bricker)	5		5	
	Orthotopic (J-pouch)	1		2	
	Other	1		0	

Biography

Dr. Mariya Berkut was born in Kazakhstan in 1991, Karaganda and is a graduate of Karaganda State Medical University. From 2015 to 2020, she completed a fellowship at the leading oncology center in St. Petersburg, Russia-N.N. Petrov National Medical Research Center of oncology. He obtained her medical degree at the same place. At the moment Dr. Berkut works as a surgical oncologist, treats tumor diseases of the genitourinary system, including the use of minimally invasive surgery (owns laparoscopic and robot-assisted technique). The area of interest is related to improving the results of treatment patients with bladder, reducing the incidence of complications and improving the patient's quality of life. She also is a member of the EAU and ESMO. In addition, she studies the Italian language, cuisine and traditions.

Molecular Pathways Involved in Prolactin-Dependent JAK2/PAK1 Action: Implication in Breast Cancer

Dr. Maria Diakonova

Department of Biological Sciences, University of Toledo, OH, USA

Abstract

Background/problem: Although the significance of hormone prolactin (PRL) and serine threonine kinase PAK1 in breast cancer is widely acknowledged, the mechanisms of their action remain poorly understood. Objectives: We previously demonstrated that PAK1 is a novel substrate of the JAK2 tyrosine kinase and that JAK2, activated by PRL phosphorylates PAK1 in vivo and in vitro. Methodology: PAK1 tyrosines 153, 201 and 285 were identified as sites of JAK2 tyrosyl phosphorylation (pTyr-PAK1) by mass spectrometry and two-dimensional peptide mapping. Using phosphospecific antibodies directed to single phosphorylated tyrosines on PAK1, we identified Tyr285 as a site of PRL-dependent phosphorylation of PAK1 by JAK2 Results: We found that pTyr-PAK1 facilitates PRL-dependent motility of breast cancer cells via at least two mechanisms: (1) formation of paxillin/ GIT1/ βPIX /pTyr-PAK1 complexes resulting in increased adhesion turnover and (2) phosphorylation of actin-binding protein filamin A. Increased adhesion turnover is the basis for cell migration and phosphorylatedfilamin A stimulates the kinase activity of PAK1 to facilitate cell motility. pTyr-PAK1 also stimulates invasion of breast cancer cells in response to PRL and 3D-collagen IV via transcription and secretion of MMP-1 and MMP-3 in a MAPK-dependent manner. In support, using pTyr-specific AB, our ICH analysis of human microarray tissue revealed that PAK1 tyrosyl phosphorylation on Tyr285 is higher in breast carcinomas than in normal breast tissue suggesting that pTyr285-PAK1 may modulate PAK1 signaling during tumor progression. We have also shown that that pTyr-PAK1 enhances breast tumor growth and metastasis in a xenograft mouse model. Next, although PRL and estrogen exert independent effect on breast cancer cells, there is cross-talk between these two hormones that leads to breast cancer progression. We have provided evidences that pTyr-PAK1is a common node for estrogen- and PRL-dependent pathways. We showed that the estrogen-activated cytoplasmic kinase Etk directly phosphorylates PAK1 on Tyr153. We also demonstrated that PKA phosphorylates Ser305 on estrogen receptor (ERα) in response to estrogen, but pTyr-PAK1 phosphorylates Ser305-ERα in response to PRL, implying that maximal ERα phosphorylation is achieved when cells are exposed to both PRL and estrogen. Conclusions: Overall, our data illustrate the complex interaction between prolactin and the cell microenvironment in breast cancer cells and suggest a pivotal role for prolactin/JAK2/pTyr-PAK1 signaling in breast cancer metastasis. Additionally, our data strongly support a critical interplay between PRL and estrogen via PAK1 and suggest that ligand-independent activation of estrogen receptor through PRL/PAK1 may impart resistance to anti-estrogen therapies.

Biography

Upon completion of her doctorate in Cell Biology in the Institute of Cytology Russian Academy of Science, she started her postdoctoral training at the European Molecular Biology Laboratory (EMBL) in Heidelberg, Germany. She continued her postdoctoral training at the University of Michigan where she studied growth hormone-dependent signal transduction. She joined the Department of Biological Sciences at the University of Toledo, OH as Assistant Professor in 2006 promoted to Associate Professor in 2012 and to Professor in 2018. She directs research focusing on a role of prolactin and estrogen in breast cancer progression. She has demonstrated that the serine-threonine kinase PAK1 associates with and is tyrosyl phosphorylated by prolactin-activated JAK2 kinase to regulate cyclin D1 promoter activity, adhesion, motility and invasiveness of breast cancer cells by multiple mechanisms. She has also demonstrated that JAK2 tyrosine kinase specifically associated with centrosomes where it binds to ninein. Her current research focuses on a role of PAK1 in prolactin and estrogen signaling. She has published more than 30 papers in reputed journals and has served as lead editor of “Recent Advances in Prolactin Research” book (Springer).

Pathology of the Gastrointestinal Tract in Children as a Manifestation of the Late Toxic Effect of Anticancer Therapy

Gelfer S.A, Zhukovskaya E.V, Karelin A.F

Dmitry Rogachev National Medical Research Center Of Pediatric Hematology, Oncology and Immunology, Russia

Abstract

Introduction. All over the world there is a trend towards an increase in the incidence of cancer in the child population. The defeat of the gastrointestinal tract (GIT) system is the most common complication of anticancer treatment in children. Pathology from the gastrointestinal tract can occur in any of its departments. Despite the great regenerative capacity of the child's body, not all patients have a complete restoration of damaged tissue. Thus, the GIT system often remains altered in remission after completion of treatment. Purpose of work: to study the spread of pathology of the gastrointestinal tract in children who completed anticancer therapy. Materials and methods. The study was conducted on the basis of the Russian Clinical Rehabilitation Research Center "Russkoye pole". For the period of 3 years 2017-2019, 248 case histories of patients with hemoblastoses were analyzed. The average age was 10.5 years, the average duration of remission was 5.5 years, there were 140 (56.2%) boys and 109 (43.8%) girls. The study was retrospective. Results. As a result of the study, GIT pathology was detected in 167 (67.9%) patients. The frequency of diagnosing the gastrointestinal tract in boys is 2 times higher than in girls. The dependence of the incidence of GIT on the duration of remission in this group of patients was not revealed. Violation of the nutritional status in the form of overweight was detected in 96 (57%) children, 58 boys, 38 girls with gastrointestinal disorders, the average age of which was 11 (±1.2 years), of which 24 children, 16 boys and 8 girls were obese. Violation in metabolic homeostasis included an increase in bilirubin, more often direct, transaminases, amylase, cholesterol; during ultrasound examination - hepatomegaly, enlargement of the spleen, diffuse changes in the parenchyma of the liver and spleen, anomalies of the gallbladder, suspension in the gallbladder. Gastroscopy revealed manifestations of gastritis in various degrees of severity, a single ulcerative process. The pathology of GIT in most patients is combined with: functional disorders of the stomach, pancreatitis, a symptom of irritable bowel (IBS). In 80% of children with gastrointestinal pathology, there are deviations from the teeth and oral mucosa. Conclusions. Long-term effects of antitumor therapy of hemoblastoses in children and adolescents affect the gastrointestinal tract. At risk are patients aged 10 to 14 years. Changes in nutritional status are among the most common manifestations of gastrointestinal dysfunction. Given the high incidence of gastrointestinal pathology (67.9%) and the variety of complaints, the non-specificity of clinical manifestations, it is necessary to actively diagnose the gastrointestinal system at the stages of rehabilitation and monitoring the effectiveness of the rehabilitation measures taken.

Biography

Gelfer Svetlana graduated from Pirogov Russian National Research Medical University in 2009. She graduated from the residency in neonatology in 2014, internship in pediatrics in 2016. She is a pediatrician in Clinical Rehabilitation Research Center for patients in remission “Russkoye pole” of Dmitry Rogachev National Medical Research Center Of Pediatric Hematology, Oncology and Immunology. Since 2017, studies the late toxic effects of anti-cancer therapy. She has several publications in Russian scientific journals. She spoke at cancer research conferences in Moscow, St. Petersburg, Las Vegas and Sochi.

Phase I Study of Adjuvant Immunotherapy with Autologous Tumor-infiltrating Lymphocytes in locally Advanced Cervical Cancer

He Huang[1,3], Cai-ping Nie[1,2], Xiu-feng Liu[1,2], Bin Song[6,7], Jian-hui Yue[6,8], Jing-xiao Xu[1,2], Jia He[1,2], Kui Li[1,2], Yan-lin Feng[1,3], Ting Wan[1,3], Min Zheng[1,3], Yan-Na Zhang[1,3], Wei-Jun Ye[1,4], Jun-Dong Li[1,3], Yan-Fang Li[1,3], Jun-yun Li[1,4], Xin-Ping Cao[1,4], Zhi-min Liu[1,3], Xiao-shi Zhang[1,2], Qing Liu[1,6], Xi Zhang[6], Ji-Hong Liu[1,3], Jiang Li[1,2]

1. State Key Laboratory of Oncology in South China; Collaborative Innovation Center for Cancer Medicine, China
2. Department of Biotherapy, Sun Yat-sen University Cancer Center, China
3. Department of Gynecological Oncology, Sun Yat-sen University Cancer Center, China
4. Department of Radiation Oncology, Sun Yat-sen University Cancer Center, China
5. Department of Cancer Prevention Research, Sun Yat-sen University Cancer Center, China
6. BGI-Shenzhen, Shenzhen, China
7. College of Life Sciences, University of Chinese Academy of Sciences, Beijing, China
8. Section of Cell Biology and Physiology, Department of Biology, University of Copenhagen, Copenhagen, Den mark

Abstract

Background: Adoptive cell therapy (ACT) with tumor-infiltrating lymphocytes (TILs) has achieved remarkable clinical efficacy in metastatic cancers such as melanoma and cervical cancer (CC). Here we explored the safety, feasibility and preliminary tumor response and performed translational investigations of adjuvant immunotherapy using infusion of autogenous (auto)-TILs following concurrent chemoradiotherapy (CCRT) in CC patients with locally advanced disease. Methods: Twenty-seven CC patients with stage III to IV disease were recruited in this single-center, phase I study. TILs were isolated from lesions in the uterine cervix and generated under good manufacturing practices (GMP) conditions and then infused after CCRT plus intramuscular interleukin (IL)-2 injections. Results: TILs from 20 of the 27 patients were successfully expanded, with a feasibility of 74.1%. Twelve patients received TILs following CCRT. Adverse events (AEs) were primarily attributable to CCRT. Only 1 (8.3%) patient experienced severe toxicity with a grade 3 hypersensitivity reaction after TIL infusion. No autoimmune AEs, such as pneumonitis, hepatitis, or myocarditis, occurred, and there was no treatment-related mortality. Nine of 12 patients (75.0%) attained complete response, with a disease control duration of 9 to 22 months. Translational investigation showed that the transcriptomic characteristics of the infused TIL products and some immune biomarkers in the tumor microenvironment and serum of CC patients at baseline were correlated with the clinical response. Conclusion: TIL-based ACT following CCRT was safe in an academic center setting, with potential effective responses in locally advanced CC patients. 'Hot' inflammatory immune environments are beneficial to the clinical efficacy of TIL-based ACT as adjuvant therapy.

Biography

Jiang Li MD, PhD is a Professor at Biotherapy Center, Cancer Centre, Sun Yat-Sen University, China. Dr. Li is focused on the immune escape of tumor microenvironment and adoptive immunotherapy based on T cells for solid cancers. Nasopharyngeal carcinoma (NPC) is associated with EBV infection with a high incidence in South China and South Asia, which is a good model for T-cell based on immunotherapy. She managed the phase I and phase II study of adoptive T cell transferred immunotherapy based on ex vivo reactivated tumor-infiltrating lymphocytes (TIL) combined with concurrent chemoradiotherapy (CCRT) for advanced NPC patients, now the phase II study has been finished, and all data is following up and prepared for publication. In addition, a phase I study for auto-TIL following CCRT treatment for advanced cervical patients has been finished in 2021 (JCI, 2022). Moreover, the mechanism of T cell-based immunosuppression for tumor escape in virus associated tumors is the main researcher direction in her lab now. Recently, she has been published her work on JCI, Cell Death & Differentiation, Oncogene, Plos Pathogens and et al peer review journals.

Enhance Nanoparticles and Drug Deliveries in Tumor Using E.Coli Phagelysates

Fridon Shubitidze, Ph.D, Ketevan Ghambashidze[2], P. Jack Hoopes[1,3]

1. Professor of Engineering, Thayer School of Engineering, Dartmouth College, USA
2. Tbilisi State Medical University, USA
3. Geisel School of Medicine at Dartmouth College, USA

Abstract

The relationship between tumors and the microenvironment, or TME, is complex and dynamic. Tumors and the TME interact constantly, with each influencing the other in various ways. Tumors can release extracellular signals that alter the microenvironment, promoting angiogenesis (the growth of new blood vessels) and inducing immune tolerance (the suppression of the immune system's response to the tumor). At the same time, the immune cells in the microenvironment can affect the growth and progression of cancer cells. Recent studies have showed that E. coli phagelysate (EcPHL) can modify the tumor microenvironment, by promoting the development of M1-polarized macrophages which are more tumoricidal. In this study, the effects of EcPHL vaccination on the tumor microenvironment and magnetic nanoparticle (MNP) distribution in mice with Ehrlich adenocarcinoma tumors are analyzed. The results show that the EcPHL vaccination has an anti-tumor effect, reducing the growth rate of the tumors and improving the distribution of MNPs within the tumors. These findings suggest that the combination of EcPHL vaccination and MNPH therapy may be an effective approach for improving drugs and MNP delivery in the cancer.

Biography

Fridon Shubitidze is currently working as Professor of Engineering in Dartmouth College, USA. His areas of interest are Numerical methods in computational electromagnetics; electromagnetic sensing methodologies; detection and discrimination of sub-surface objects; linear and non-linear inverse-scattering; induced geo-electromagnetic fields; micro strip antennas; photonic band gaps; near field optics; DNA sequencing; electrostatic discharge; magnetic nano-particles hyperthermia for cancer treatment and imaging

Demographics and Clinical Characteristics Associated with Course Completion of a Web-based Llifestyle Educational Program for People with Multiple Sclerosis

Nayana Kulkarni[*1], Sirshendu Roy[2], Aditya Adhav[2], Ravindra Tandale[1], Shital Patil[1], Nishtha Paleja[3], Yasam Venkata Ramesh[4], Raj Nagarkar[2]

1. Department of Anaesthesiology, HCG Manavata Cancer Centre, India

2. Department of Surgical Oncology, HCG Manavata Cancer Centre, India

3. Department of Medical Research, HCG Manavata Cancer Centre, India

4. Department of Academics, HCG Manavata Cancer Centre, India

Abstract

Background: The relationship between breast cancer surgeries (BCS) and their associated extreme pain is unavoidable. In such cases, the use of clonidine as an adjuvant with general anaesthesia was highly recommended to improve the overall quality of recovery by reducing post-operative pain and potential indications. Objectives: In this randomised, prospective, double-blinded interventional study, the effectiveness of clonidine and its outcomes in providing balanced anaesthesia in patients who underwent BCS were studied and reported. Methodology: A total of 80 patients met our inclusion and exclusion criteria. Post-inclusion, all the patients were divided into two randomly assigned groups: placebo (n=40, balanced general anaesthesia alone) and clonidine (n = 40, clonidine as an adjuvant followed by balanced general anaesthesia). Results: Of 80 patients, the median age in both arms was 47 ± 2 years. The pre-/post-induction heart rate (HR) and mean arterial pressure (MAP) of the patients from the clonidine arm (78 bpm, 105 mmHg and 83bpm, 81mmHg) and placebo arm (82 bpm, 103 mmHg and 91bpm, 90mmHg) were noted. From post-surgical sedation scores at 1 h, 2 h, and 6 h, it was noticed that a total of 7 patients were seen to be agitated (1 of the clonidine arm and 6 of the placebo arm). Intraoperative additional analgesic (fentanyl) and β-blocker (labetalol) requirement was reported to be significant and observed to be more in the placebo arm (34 and 35) over clonidine arm (2 and 3) patients, $P<0.001$. Whereas the post-operative pain score (after 6h) and surgical field score (excellent, 32) were well maintained in the clonidine arm over the placebo arm. The most common noticeable post-operative side effects such as nausea and vomiting (PONV, n=11) were found to be more inthe placebo arm. Whereas the patients from the clonidine arm were found to have a better quality of recovery. Conclusions: Clonidine as an adjuvant provided better intra-/postoperative analgesia by prolonging the duration of anaesthesia without major hemodynamic alteration and side effects. Overall, the use of clonidine as an adjuvant was observed to be safe and cost-effective in patients undergoing BCS.

Biography

Dr. Nayana Chandrashekhar Kulkarni is the Head of the Department of Anesthesiology, HCG Manavata Cancer Centre, India. Also she is consultant anesthesiologist at HCG Manavata Curie Cancer Centre from March 2008 till date. She earned her MBBS and MD degree from Byramjjee jeejeeghoy medical college, Pune. She has over 30 papers presented at both national and international conferences.

How the COVID-19 pandemic could affect the quality of life in children with malignant

Elena V. Zhukovskaya[1], Alexander F. Karelin[1]

1.Dmitry Rogachev National Medical Research Center of Pediatric Hematology, Oncology and Immunology, Moscow, Russia

Abstract

The COVID-19 pandemic is affecting the somatic and mental health of the population globally. Patients with oncological pathology formed a risk group with severe complications of COVID-19. Aim of the study was to estimate the quality of life (QOL)in children and adolescents after completion of anticancer therapy in a pandemic. Materials and methods. A retrospective monocentral cross-sectional study was performed at the medical and rehabilitation scientific center ;Russian Field; in 2022. The comparison groups were formed by random sampling from among patients with malignant neoplasms and severe pathology of hematopoiesis. 246 patients were hospitalized from January 01 to June 30, 2019; no COVID-19 cases were registered in Russia during this period. The Control group included 242 patients matched by sex and age, hospitalized from January 01 to June 30, 2021, which corresponds to the period of epidemic trouble. The questionnaire PedsQL 4,0 consists of 23 questions [1]. We used descriptive statistics for continuous data, to compare the indicators of quality of life in children in groups - paired Studen t-test. Results. According to the site http://stopcoronarus.rf, in our group incidence of COVID-19 was 156,2/100, it's 10 times higher than in healthy population 7-14 years old. QOL in cancer patients was lower in pandemic, than onset of COVID-19. The reasons for lower QOL parameters, in our opinion: high incidence of COVID-19 among patients; consequences of a coronovirus infection; realization of symptoms of psychosomatic distress; quarantine measures leading to the formation of the effects of physical inactivity. All the problems can be effectively addressed with adequate guidance for parents and/or community structures. The negative impact of the COVID-19 pandemic on the parents of our patients turned out to be less significant than one might expect. According to the authors of a large study, which received similar results, a child's cancer is a central trigger for parents, which
means that an additional, global stressor does not cause a deeper deterioration in their well-being [2]. Conclusion. Children in remission of malignant tumors and their parents noted lower rates of QOL in the conditions of the pandemic than before it began. Gender differences are realized in higher QOL in boys compared to girls of the second age category. Children demonstrate a more negative impact of the COVID-19 coronavirus pandemic compared to the QOL estimates made by their parents. Rehabilitation programs during a pandemic should take into account not only the possibility of the formation of late toxic effects of antitumor therapy, but also additional stress effects on COVID-19 patients and develop programs to reduce the negative impact of the
pandemic.

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i-Biomarker CaDx Detects 99-100% of Lung Cancers

Alexandru Floares*[1], Adrian Zety[1], Eduardo Kreutz[1], George Calin[2], Carmen Floares[1], Florin Manolache[3]

1.Artificial Intelligence Expert, Cluj-Napoca, RO

2. MD Anderson Cancer Center, Houston, TX

3. Carnegie Mellon University, Pittsburgh, PA

Abstract

Background. Non-invasive, highly accurate early cancer detection dramatically impacts the cost-effectiveness of the treatment. Various liquid biopsy tests have poor/modest detection rates, because: 1) The chosen molecular alterations (e.g., circulating free DNA methylation) are not informative enough (16,8% accuracy for stage I, and 40.4% for stage II - GRAIL test); 2) The size of the inputs is too high, e.g., ~800K methylation sites or ;1M DNA fragments (fragmentomics); 3) Aggressive feature selection which results in models/tests that do not generalize well. Circulating miRNA is a good choice, as it is informative, and the input size is about 2500. Objective: Develop a non-invasive Multi Cancer Early Detection (MCED) capable of detecting lung cancer, besides other types, with the highest accuracy.
Methods. Our MCED test (i-Biomarker™ CaDx; patent pending), works on 13 cancer types with 99-100% accuracy. Here we will focus on Lung Cancer. I-Biomarker™ is technology agnostic, working on NGS, Microarray, PCR, and Nanostring circulating miRNA profiles.
We illustrate the technology on a microarray freely available dataset (GEO: GSE137140). We standardized the miRNA expression to mean = 0 and the standard deviation = 1. Besides other advantages, standardized profiles are easy to interpret - positive/negative values mean increased/decreased. We used a model amalgamation to train multiple classification algorithms, performed hyperparameter optimization, and combine the best with different weights into a final model. This increased the accuracy to 100% and, even more important, by increasing the subset of relevant miRNAs, made the test generalize well to new patients. We used Explainable AI (XAI) to explain the miRNA alteration supporting the diagnosis, both at the population and the individual (personalized) level. By mapping the population/individual miRNA alteration to the mRNA targets, and pathways, our test offers a mechanistic explanation at the population/individual level. Results. Some individual models (e.g., Ensemble of Decision Trees, Neural Networks) already reach>99%. However, integrating them with different weights into a final model increases accuracy to 100%. Furthermore, the performance is robust, as can be achieved by repeatedly changing the train/validation/test set. Using XAI, we can show the miRNA alterations explaining or supporting the diagnosis at the population and individual (personalized) levels. Conclusions. With its 99-100% accuracy (for Lung Cancer here), I-Biomarker outperforms all other cancer detection tests, including the newly proposed liquid biopsy-based ones.

Keywords: Multi-Cancer Early Detection, Lung cancer, Circulating miRNA, Non-invasive, Artificial Intelligence

E poster

Autologous Heterotopic Fresh Ovarian Graft in Woman with LACC Eligible for Pelvic Radiotherapy Treatment

Bertolazzi MA, Genta Mlnd, Baracat EC, Carvalho JP

1. Departament of Gynecology, Instituto do Cancer do Estado de Sao Paulo, Brazil

Abstract

Background: Pelvic chemoradiotherapy (CRT) is an effective treatment for Locally Advanced Cervical Cancer (LACC). However, CRT induces premature ovarian failure ceasing the production of ovarian hormones. This may lead to severe consequences to the patient's life quality, sexuality and overall healthy. An acceptable treatment to minimize the adverse effects caused by the lack of ovarian hormones is hormonal replacement but less than 40% of the patients younger than 50 years have access to this treatment. A second alternative treatment is ovarian transposing which is a surgical technique with variable success rate depending on how far the ovaries are from the radiotherapy field. A third, more promising, alternative is involves using autologous ovarian tissue as a graft in tissues far from the radiotherapy field. This treatment has the potential of maintaining the natural ovarian hormones production at a lower-cost and requiring a simpler procedure. Objective: The primary objective of this randomized phase 1-2 clinical trial is to validate the feasibility of ovarian tissue engraft into fatty tissue and its endocrine functionality. Methodology: Before the beginning of pelvic radiotherapy, one of the ovaries will be removed by laparoscopy. Ovary slices of 1-2 mm will be prepared in sterile environment and engrafted in the fatty tissue of inner tight. One representative fragment will undergo histologic evaluation. These procedures will be done in the same surgical time. Procedure: Ovarian graft Before the beginning of pelvic radiotherapy, one of the ovaries will be removed by laparoscopy. Ovary slices of 1-2 mm will be prepared in sterile environment and engrafted in the fatty tissue of inner tight. One representative fragment will undergo histologic evaluation. These procedures will be done in the same surgical time. Sample: 20 Patients, 10 in each arm (control and intervention group). Follow-up: Periodic evaluation of the following parameters at baseline and post radiotherapy (2, 6, 12 and 24 months): -Serum levels of follicle stimulating hormone (FSH) in mUI/ml and estradiol in pg/ml. Endocrine functionality is defined as FSH levels under 25 mUI/ml and estradiol upper 47 pg/mL.-Glucose, glycated hemoglobin, cholesterol, triglycerides. -Score life quality in European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ C30), Periodic evaluation of the following parameters at baseline and post radiotherapy (12 and 24 months): -Bone mineral density (BMD) in femoral neck and lumbar spine by bone densitometry, bioimpedance monitoring, quantification of body mass index. -Score life quality in European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ C30) and Score life quality in European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 Cervical Cancer Module (EORTC QLQ C30 CX24). Results: This trial is in recruiting phase.

We wish to meet you again at our upcoming conference

2nd Edition of Cancer Clinical Trials Conference Septemner 13-14, 2023, Madrid, Spain

Questions - Contact us
daisy@cilnconf.com

Abstract Book of the 1st CRCT Meeting
Dubai, March 16, 2023

Thank you