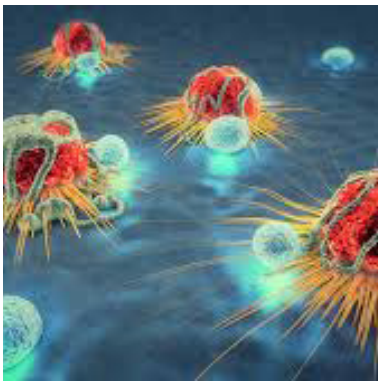
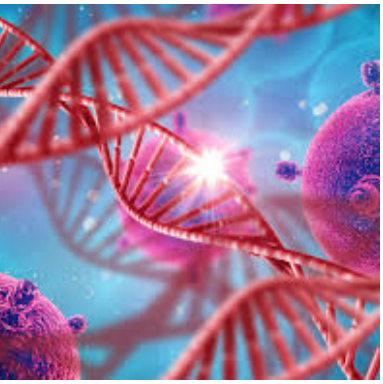
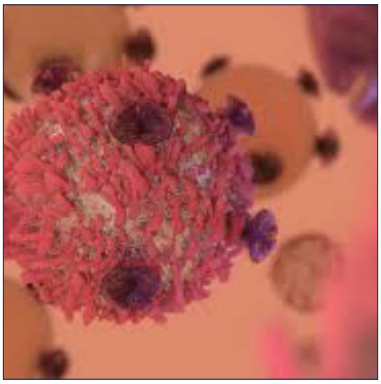
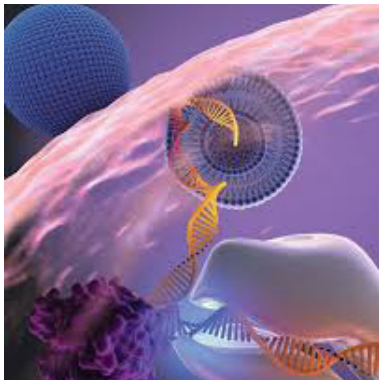
Poster

Oncology 2019 & Cancer Therapy 2019



International Conference on

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March 18-19, 2019 | London, UK

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Radiation response of cancer stem cells as predictive marker of radiotherapy efficiency in cervical cancer patients

Zamulaeva Irina A
A Tsyb Medical Radiological Research Centre, Russia

Radioresistance of cancer stem cells (CSCs) is considered as one of the possible causes of cancer recurrence after radiation therapy. However, little is known about quantitative changes in CSC subpopulation after radiation exposure under clinical conditions and association of these changes with the efficiency of treatment of various malignancies including squamous cell carcinoma of uterine cervix (SCCUC). Therefore, the aim of this study was to evaluate changes in proportion of CSCs in cervical scrape samples from SCCUC patients after the first few sessions of radiotherapy and compare these changes with short-term outcomes of the full course of the treatment including external and intracavitary irradiation. The degree of tumor regression was assessed 3-6 months after the treatment. Study group consisted of 34 patients at FIGO stages IB-IVA. Informed consent was obtained from all patients. Proportion of $CD44^{+}CD24^{low}$ CSCs was determined by FACS analysis before the treatment and 24 hours after low-LET radiation exposure at a cumulative dose of 10 Gy to point A. Postradiation decrease in the CSC proportion was associated with the complete tumor regression, while increase – with the partial regression. Thus, the frequency of the partial tumor regression was 5,6-fold higher in patients with postradiation increase in the CSC proportion than in other patients who demonstrated decrease in this indicator (p=0.04, AUC=0.73). The results demonstrated predictive value of individual radiation response of the CSC population for short-term outcomes of SCCUC treatment.

This work was supported by grant of Russian Scientific Foundation # 18-75-10025.

Speaker Biography

Zamulaeva Irina A has completed her PhD at the age of 32 years from Medical Radiological Research Centre, Russia. She is professor and Head of Department of Radiation Biochemistry of Medical Radiological Research Centre. She has over 140 publications (in English and Russian) that have been cited over 600 times, and her publication H-index is 11 according to Russian Science Citation Index. She has been serving as an editorial board member of reputed Journals.

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Notes:

Radioresistance of breast cancer stem cells after single-dose and fractionated γ-radiation exposure and radiosensitizing effect of dimeric bisbenzimidazoles *in vitro*

Matchuk Olga N, Churyukina K A, Zhuze A L and **Zamulaeva I A**
A Tsyb Medical Radiological Research Center, Russia

Numerous studies have proven the high resistance of cancer stem cells (CSCs) to a single-dose low-LET ionizing radiation exposure in vitro. However, the patterns and mechanisms of fractionated radiation effects on this population of cells have not been studied enough. The aim of the study was to elucidate effects of single-dose and fractionated γ-radiation exposure on CSCs of breast adenocarcinoma line MCF-7 and reveal means for CSC radio sensitization by inhibition of DNA damage repair. CSCs were isolated as $CD44^{+}CD24^{low/-}$ cells or side population (SP) by flow cytometry. Both methods were used to show a statistically significant increase in the relative and absolute number of CSCs both after single-dose and fractionated irradiation at doses of 4 Gy and more. These data were the basis for further work in order to reduce the resistance of CSCs in the range of 4-6 Gy. Synthetic dimeric bisbenzimidazoles – DB(n) that specifically bind to DNA A-T enriched sequences and inhibit a number of enzymes involved in chromatin remodeling and repair of DNA damages were synthesized. In our experiments length of oligomethylene linker (n) between two bisbenzimidazole blocks ranged from 1 to 11. DB (5) and DB (7) in combination with irradiation significantly reduced the proportion and clonogenic ability of CSCs compared with those after radiation exposure ($p<0.05$). The coefficients of the synergistic effect of these compounds and radiation on CSC clonogenicity were 1.3 for DB (5) and 1.2 for DB (7). Thus, the results showed that DB (5) and DB (7) could be used to develop anticancer drugs for elimination of CSCs and increase the effectiveness of cancer patient radiotherapy.

This work was supported by grant of Russian Scientific Foundation # 18-75-10025.

Speaker Biography

Matchuk Olga N has completed her PhD from A. Tsyb Medical Radiological Research Center, Russia in 2016. She is senior researcher of Laboratory of Radiation Biochemistry of Medical Radiological Research Center. She has over 50 publications (in English and Russian) that have been cited over 90 times, and her publication H-index (Scopus) is 4.

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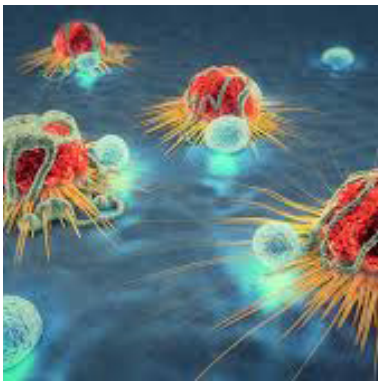
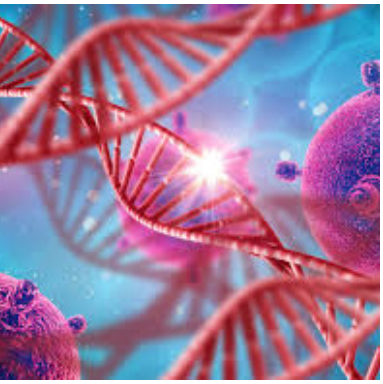
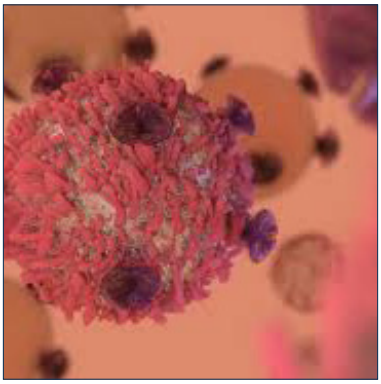
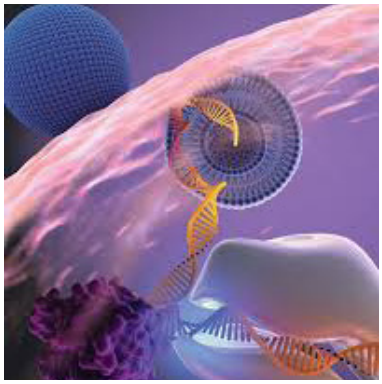
Video Presentation

Oncology 2019 & Cancer Therapy 2019



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Knowledge-based image analysis algorithms for quantifying complexity in histology and MR/CT data

David H Nguyen
Stanford University, USA

Current feature-based image analysis algorithms can identify nuclei, cytoplasm, and stroma. These algorithms can also detect normal tissue versus neoplastic lesions. However, feature-based algorithms cannot detect the higher-level morphological patterns in tumors that are reminiscent of the tissue of origin. Furthermore, these algorithms cannot detect the degree of recurring sub- architectures that exist in tumors of the same type or stage (i.e. the degree of partial rosettes, the degree of subtle cellular alignments). These recurring sub- architectures in tumors can be precisely quantified by knowledge-based algorithms that capture the spatial information in normal tissues. The knowledge-based algorithms being referenced are publicly available online (ArXiv ID's: 1801.06752, 1710.06593, 1704.07571, 1704.07567, 1704.07567). Some of these algorithms are also applicable to quantifying subtilties in spatial information that are present in magnetic resonance (MR) and computed tomography (CT) images (ArXiv ID: 1801.06752), which may be useful for refining clinical classification of specimens.

Speaker Biography

David H Nguyen is a tumor biologist developing image analysis algorithms to advance digital pathology for cancer diagnostics. His algorithms quantify knowledge-based features of tissue architecture so they can be included in machine learning models that predict clinical outcome. Dave obtained his B.A. and PhD from the University of California, Berkeley. He is currently a Visiting Scholar in the Department of Radiology at Stanford University. Prior to this, he was an Affiliate Scientist in the Molecular Biophysics and Integrated Bioimaging Division at Lawrence Berkeley National Laboratory. His research interests are on Cancer Biology, Immunohistochemistry, Cancer Cell Biology, Cancer, Tumors, Image Analysis, Tumor Biology, Ionizing Radiation, Tumor Microenvironment, Digital Image Analysis, computational pathology.

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Measles virus is associated with classic Hodgkin lymphoma and additional cancers - A never ending saga

Daniel Benharroch
Soroka University Medical Center and Ben Gurion University of the Negev, Israel

The suggestion of a relationship between the measles virus and classic Hodgkin lymphoma was first presented by our laboratory in 2003. Four years later, our hypothesis was refuted conjointly by two European groups. However, our reevaluation of the proposed arguments allowed us to carry on with our line of research. By that time, we submitted evidence of associations between the measles virus and several further solid tumors, including lung and breast cancers. Modulation of apoptosis was later proposed as a possible mechanism in the oncogenesis of classic Hodgkin lymphoma. Measles virotherapy has been excluded from our discussion. Additional evidence has been compiled in the form of Western blots of lung cancers, and of a tissue micro-array in four categories of cancer. The possible role of atypical measles syndrome in cancer, which although a rare condition, but still prevalent, is discussed in the context of immune waning. Since measles virus and EBV expression were displayed in various combinations, we raise the possibility that their net consequences on tumor cell apoptosis in classic Hodgkin lymphoma, might originate from opposing effects from the two viruses.

Speaker Biography

Daniel Benharroch started his career as an Intern at the Soroka University Medical Center in Isreal in the year 1976. Post his internship, he worked as a resident at the Soroka University Medical Center for several years. Over his career he has been a member of various associations like The Israel Medical Association, The Israel Society of Pathology, The International Academy of Pathology, The European Association of Cancer Research, The Israel Association of Hematology, The European Hematology Association. He also served as a member of Editorial Boeard or reviewer for journals of Clinico-Pathological Conferences in "Harefuah", Leukemia & Lymphoma, Acta Hematologica, The Indian Journal of Cancer. He has taught various courses in numerous universities and is currently serving as a Full Professor of Pathology at The Ben-Gurion University of the Negev in Israel.

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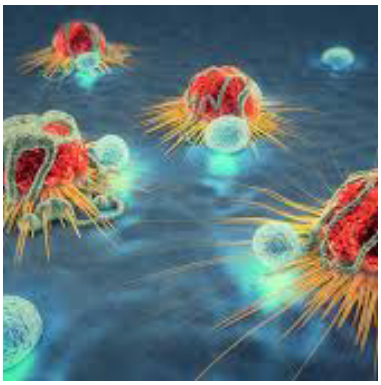
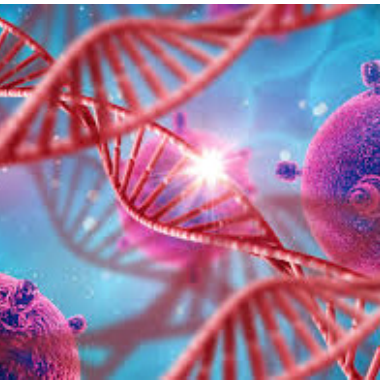
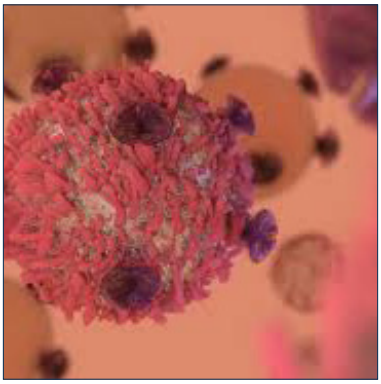
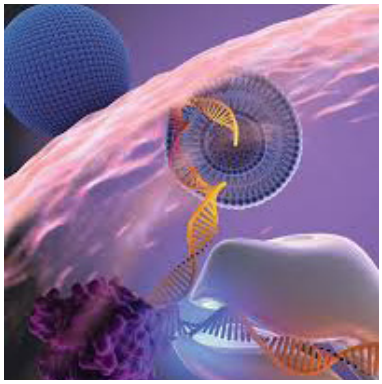
Accepted Abstracts

Oncology 2019 & Cancer Therapy 2019



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Reduction of breast cancer relapses with perioperative non-steroidal anti-inflammatory drugs: New findings and a review

Michael Retsky
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A bimodal pattern of hazard of relapse among early stage breast cancer patients has been identified in multiple databases. Using computer simulation and access to a very high quality database from Milan for patients treated with mastectomy only, we proposed that relapses within 3 years of surgery are stimulated somehow by the surgical procedure. Retrospective breast cancer data from a Brussels anesthesiology group suggested a plausible mechanism. Use of ketorolac, a common NSAID analgesic used before surgery was associated with far superior disease-free survival. The expected prominent early relapse events in months 9-18 are reduced 5-fold. Transient systemic inflammation accompanying surgery (identified by IL-6 in serum) could facilitate angiogenesis of dormant micrometastases and proliferation of dormant single cells and could have been effectively blocked by the perioperative NSAID. If this observation holds up to further scrutiny, it could mean that the simple use of this safe, inexpensive and effective anti-inflammatory agent at surgery might eliminate early relapses and reduce mortality by 25 to 50%. This hypothesis has been recently confirmed in a mouse model by Krall et al in Science Translational Medicine 2018 and a second retrospective study by Desmedt et al in JNCI 2018. Post-operative bleeding is a major concern with perioperative NSAIDs however tranexamic acid has been found to reduce such bleeding by 39% in a clinical trial by Ausen et al in BJ Surg 2018.

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Novel mechanism of the cervical carcinogenesis

Cheng Wang
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HPV infections are common in healthy women but only rarely cause cervical cancer, suggesting that individual genetic susceptibility may play a critical role in the establishment of persistent HPV infection and development of cervical cancer. We provide convincing *in vitro* and *in vivo* evidence showing that disruption of the Hippo pathway and subsequent hyperactivation of *YAP1* oncogene is a critical pathological event that determines individual susceptibility to HPV infection and cervical carcinogenesis. We found that hyperactivation of YAP1 in mouse cervical epithelium was sufficient to induce malignant transformation of cervical epithelial cells and promote development of invasive cervical cancer. Cervical epithelial cell-specific HPV16 E6/E7 and YAP1 double knock-in mouse model demonstrated that HPV synergized with hyperactivated YAP1 to promote the initiation and progression of cervical cancer. Our mechanistic studies indicated that hyperactivation of YAP1 in cervical epithelial cells facilitated HPV infection via increasing the putative HPV receptor molecules and disrupting the host cell innate immunity. Our finding challenges the dogma that HPV is a necessary agent for the development of cervical cancer, uncovers a novel mechanism for the cervical carcinogenesis, and provides new targets for developing strategies to improve prevention and treatment of cervical cancer.

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The value of contrast enhanced ultrasound in the location of sentinel lymph node in breast cancer

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Sentinel lymph node (SLN) location and biopsy was designed to minimize side effects of axillary dissection with equivalent outcomes.

Objective: To explore the detection rate and the accuracy of sentinel lymph node (SLN) in breast cancer by percutaneous injection of ultrasound contrast agent in mammary areola region.

Methods: 400 breast cancer patients in our breast surgery department from July 2017 to November 2018 were involved, all patients with preoperative contrast-enhanced ultrasound (CEUS), that respectively intracutaneous injection ultrasonic contrast agent 1ml at 3,6 o 'clock and subcutaneous injection ultrasonic contrast agent 1ml at 9, 12 o 'clock. Tracing enhanced SLNs along the enhanced lymphatic vessels from mammary areola after massage for one minute. Recording the number of enhanced SLN and marking the first SLN with injecting nanocarbon into the SLN under the guidance of CEUS. Intraoperative dye method (methylene blue) was used to track SLNs and compare the results with CEUS.

Results: 395 of 400 patients with breast cancer injected with ultrasound contrast agents had detected a total of 818 enhanced SLNs (range 1-5, 2.045±1.139), the detection rate is 98.75%. In the 395 cases, 386 cases' first SLNs with the location of the CEUS matched with the first SLNs observed in the intraoperative dye method, the accuracy is 97.72%. There were 5 patients who were found interrupted lymphatic vessel and no enhanced SLN in CEUS. 3 of them, whose pathological results of axillary lymph node dissection showed that axillary lymph nodes with cancer metastasis, observed interrupted lymphatic vessel and no dyeing lymph node in the intraoperative dye method. While 2 of the 5 patients observed dyeing lymph nodes along the dyeing lymphatic vessels in the intraoperative dye method, and they didn't metastasis.

Conclusion: Percutaneous injection of ultrasound contrast agent in mammary areola region has certain application value to detect and locate the SLNs in breast cancer patient.

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Notes:

Genetic and imaging factors affecting renal cell carcinoma survival

Ecem Altay and **Albert Guvenis**
Bogazici University, Turkey

Renal cell carcinoma (RCC), the most common type of kidney cancers, is the most deadly of urological malignancies. Scientists are studying to understand the renal cell carcinoma mechanism in order to improve treatment options and to provide patients longer and higher-quality lifetime. In this research, factors that affect renal cell carcinoma survival are studied in order to shed light on controversies in the literature, and these factors are mostly mutated gene (VHL) and imaging feature (tumor stage). The Cancer Genome Atlas and The Cancer Imaging Archive were used to obtain patient genetic and imaging data. Kaplan-Meier method and log-rank test were applied to evaluate the effect of genetic and imaging factors on survival of RCC patients. The effect of presence of mutated VHL gene at different stage levels has been evaluated (P=0.602 for stage I, P=0.005 for stage IV). The results show that at stage I, VHL did not change the survival rate in our study. However, at stage IV, RCC patients who have mutated VHL gene have longer survival. Determining the factors affecting survival will help develop personalized treatments. The survival's association with therapeutic choices, image phenotypes and genetic factors follow complex relationships. It is therefore concluded that the few initial radiomics and radiogenomics studies should be pursued further. These studies have the potential to generate the reliable computer aided predictive models of survival and genetic mutations from patient image features.

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Notes:

Prognostic significance of DNMT3A mutations in patients with acute myeloid leukemia

Lamia Ibrahim
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Acute myeloid leukemia (AML) represents a heterogeneous group of malignancies with great variability in clinical course and response to therapy. Several molecular markers have been described that help to classify AML patients into risk groups. Mutations in DNA methyltransferase 3A (DNMT3A) gene were recently demonstrated in AML. Approximately 20% patients with AML carry DNMT3A gene mutations and were associated with a poor clinical outcome but its clinical implications in Egyptian AML patients are largely unknown.

The aim of the study: was to study the incidence and prognostic impact of DNMT3A mutations in patients with de novo acute myeloid leukemia.

Subjects and methods: A total of 120 patients with de novo AML were examined for mutations in DNMT3A by sequencing.

Results: DNMT3A mutations were identified in 34/120 (28%) of AML patients. 15 patients with M4, 14 patients with M5, 3 patient with M2 and 2 patient with M6. DNMT3A mutations were more frequently associated with older age, higher platelet counts and intermediate risk. DNMT3A-mutated patients did not differ regarding complete remission (CR) and disease-free survival (DFS), but had shorter overall survival (OS; P= 0.048) than DNMT3A-wild-type patients. Mutations in DNMT3A independently predicted a shorter OS (P = 0.049) by multivariate analysis.

Conclusion: We concluded that DNMT3A mutations are highly frequent in Egyptian patients with AML and are associated with an unfavorable prognosis.

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Laparoscopic proximal gastrectomy in gastro esophageal junction tumors

Ihab Ahmed
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For Siewert type I and II gastroesophageal junction tumor (GEJ) laparoscopic proximal gastrectomy can be performed. It is associated with several perioperative benefits compared with open proximal gastrectomy. The use of laparoscopic proximal gastrectomy (LPG) has become an increasingly popular approach for select tumors

Methods: We describe our technique for LPG, including the preoperative work-up, illustrated images of the main principle steps of the surgery, and our postoperative course.

Results: Thirteen pts (nine males, four female) with type I, II (GEJ) adenocarcinoma had laparoscopic radical proximal gastrectomy and D2 lymphadenectomy. All our patient received neoadjuvant chemotherapy, eleven patients had intrathoracic anastomosis through mini thoracotomy (two hand sewn end to end anastomoses and the other 9 patient end to side using circular stapler), two patients with intrathoracic anastomosis had flap and wrap technique, two patients had thoracoscopic esophageal and mediastinal lymph node dissection with cervical anastomosis

The mean blood loss 80ml, no cases were converted to open. The mean operative time 250 minute Average LN retrieved 19-25, No sever complication such as leakage, stenosis, pancreatic fistula,or intra-abdominal abscess were reported. Only One patient presented with empyema 1.5 month after discharge that was managed conservatively.

Conclusion: For carefully selected patients, LPG in GEJ tumour type I nad II is a safe and reasonable alternative for open technique, which is associated with similar oncologic outcomes and low morbidity. It showed less blood loss, respiratory infections, with similar 1- and 3-year survival rates.

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Notes:

Tumor infiltrating lymphocytes and tertiary lymphoid structure as prognostic and predictive factor for neoadjuvant chemotherapy in stage ii & iii breast cancer

Mohamed L
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Introduction: Tumor-infiltrating lymphocytes (TILs) have a strong prognostic and predictive value in triple-negative breast cancer (TNBC) and HER2 enriched subtype but no other breast subtypes but no studies have evaluated tertiary lymphoid structure (TLS).

Materials and Methods: Eighty patients with stage II and III breast cancer in Tanta oncology and pathology departments with luminal A, B and her 2 enriched and TNBC diagnosed with core needle biopsy treated with neoadjuvant chemotherapy (4 AC followed by 12-week paclitaxel + herceptin). TIL and TLS were evaluated histopathologically using hematoxylin and eosin–stained slides. The immune cell aggregates which were TLS positive showed the presence of CD20+B lymphocytes within the follicles, with areas of CD3+, CD4+ T lymphocytes mainly in the periphery [T-cell zone] resembling the highly organized structures of secondary lymphoid organs.

Results: TLS were detected in 53.7% of the tumors in whole breast groups, 83.7% in triple negative subgroup. Increased number of tumor infiltrating lymphocytes and tertiary lymphoid structure are associated with longer OS and DFS for TNBC and HER2-positive breast cancer.

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Notes:

Prognostic factors for surgical outcome and survival in women treated for borderline ovarian tumors

Mohamed Zakaria Sayer Dayer
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Data of 92 patients diagnosed with borderline ovarian tumours (BOTs) during the period from 2010 to 2017 in the National Cancer Institute (NCI), Cairo University, Egypt were retrospectively evaluated, Median follow up period was 42 months. The mean age at diagnosis was 42.7 yrs. Histopathology was serous in 63%, mucinous in 28.3%, and endometrioid in 3.3%. 65 patients (70.7%) had Stage IA disease, 17 patients had Stage IB disease (18.5%), 4 patients had Stage IC disease (4.3%), 2 patients had Stage II disease (2.2%) and 4 patients had Stage III disease (4.3%) at diagnosis. 49 patients (53.3%) underwent fertility sparing surgery, of which 19 patients underwent Unilateral ovarian cystectomy, 5 patients underwent Bilateral ovarian cystectomy, 25 underwent Unilateral salpingo-oopherectomy.43 patients (46.7%) underwent radical surgery including hysterectomy, bilateral salpingo-oopherectomy.39 patients had micropapillary disease (42 %) and 2 patients had microinvasive disease (2.2%) on histopathology.6 patients (6.5 %) had peritoneal implants of which 1 was invasive and 5 were non-invasive. Recurrence rate in the entire study group was 18.5%, 17.6% among patients underwent radical surgery and 82.4% among patients underwent fertility sparing surgery.12 of the recurrences (70.6%) were borderline whereas 5 were invasive (29.4%).Stages IA and IB had significantly higher disease free survival than other stages. Patients with micro invasion had significantly lower disease free survival 10.5 (9.52 – 11.5) Vs77.6 (70.9 – 84.1). Radical surgery had significantly higher DFS than fertility sparing surgery 75.8 (70.2 – 81.4) Vs 68.5(58.2 – 78.8).

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Notes:

Effective number of cycle and dose in metastatic castrated resistant prostatic cancer in Sudanese patient

Ehssan M Alnazir Ahmed
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Background: Prostate cancer remain the most common cancer in men worldwide. The initial treatment of choice for prostate cancer is androgen deprivation. if resistant develop then Docetaxel becomes the mainstay therapy for patients with metastatic castrated resistant prostate cancer.

Objectives: To evaluate the benefit of docetaxel in patients with metastatic castrated resistant prostate cancer (mCRPC) after initial good response to first line hormonal therapy. To determine the effective number of cycles and doses of doectaxel.

Research methodology: Study design; analytic retrospective study, Duration; 2017-2013, Area; radioisotope center of Khartoum (RICK), Population; (mCRPC). Data collection; RICK record, Inclusion criteria; any prostatic cancer patient become castrated resistant and now on docetaxel therapy

Procedure: Patient files, Sample size; 60 patients.

Conclusion: We retrospectively collected 60 patients receiving varying numbers of docetaxel plus prednislone and analyzed the clinical outcomes including performance status, prostate-specific antigen (PSA) response and pain. According to this study we found that docetaxel has effective role in the treatment of mCRPC patients with optimal number of cycles 6 to 8 every 3 weeks and dose of 75mg.

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Expression of RAS and RAB interactor 1 (RIN1) in head and neck tumours at some selected hospital in Ghana

Precious Barnes
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Background: Head and neck cancers (HNC) are cancers of the paranasal sinuses, the salivary glands and the upper aero¬digestive tract. RIN1 is a Ras effector protein regulating epithelial cell properties and has been implicated in a number of cancers.

Method: The aim of this study was to investigate the expression of RIN1 in head and neck tumour. RIN1 expression was analyzed using quantitative real-time PCR (qRT-PCR) and immunohistochemical staining on tissue samples from a consecutive series of 150 head and neck tumour patients who underwent tumor resections between 2014 and 2017.

Results: The relationship between RIN1 expressions, clinicopathological factors, was investigated. qRT-PCR results showed that the RIN1 mRNA expression was low in tumor tissue samples than in RIN1 expression were low as compared with the normal head and neck tissues. High and low Rin 1 was compared with ages ≤40, >40 in the head and neck cancer of p- value 0.02. There was a significant difference between the histological differentiation of the magninant tumour with p values of 0.001, when poor and well moderate was compared.

Conclusion: Our data suggest that RIN1 plays an important role in head and neck tumour progression and that its expression will provide baseline data to facilitate identification of new molecular targeting therapeutics.

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