

EP009 / #810

MOLECULAR PROFILING WITH SOMATIC VARIANTS IN ENDOMETRIAL CANCER

Khadra Galaal¹, Aida Alyahyaa², Aisha Al Naamani², Anooa Pullanhi¹, Shoaib Al Zad-jali¹, Huda Kashoob¹, Babikir Ahmed Ahmed¹, Mohamed Al Wahaibi¹, Hamida Al Bar-wani¹. ¹Sultan Qaboos Comprehensive Cancer Care & Research Centre- SQCCRC, Surgical Oncology, MUSCAT, Oman; ²Sultan Qaboos Comprehensive Cancer care & research centre, Research Laboratory, muscat, Oman

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Introduction: The Cancer Genome Atlas (TCGA)-based molecular classification stratifies endometrial carcinomas (EC) into four categories: POLE mutated (POLEmut), mismatch repair deficient (MMRd), p53 abnormal (p53abn) and no specific molecular profile (NSMP) with divergent prognoses. The aim of our study was to identify and characterize somatic variants in EC using FFPE in Omani women.

Methods: A retrospective study at the Sultan Qaboos Comprehensive Cancer Care and Research Center (SQCCRC) between 2022 and 2024 on the outcomes of endometrial cancer. Archived formalin-fixed paraffin-embedded samples were obtained, DNA was extracted using MagMax extraction kits. Next-generation sequencing (NGS) was utilized to investigate somatic variants in patient samples. The OncoPrint™ Comprehensive Assay Plus was used to identify genetic variants.

Results: We included 32 confirmed malignancies, DNA was extracted from FFPE in 19. The median age was 58 years (31.3-87.3), BMI was 34.8 and 67.7% presented at stage 1 and 66.7% were endometrioid adenocarcinoma, The most frequent mutation was PTEN (57.8%), PIK3CA (42%), TP53 36%, POLE was 35.7%, CTNNB1 21% and ATM 15.7%. All cases are discussed in the MDT, decision on treatment strategies was made following the implementation of molecular classification in 34% of cases and treatment approach changed.

Conclusion/Implications: Outcomes from randomized trials have shown that molecular classification has prognostic value in EC. In our study we demonstrate that molecular classification had an impact on the management of patients. We plan to expand the molecular profiling to all cases diagnosed and treated. Long-term follow-up and prognostic data are needed in our population.

EP010 / #974

UNCOVERING THE BURDEN OF VITAMIN D3 DEFICIENCY IN PATIENTS WITH NEWLY DIAGNOSED GYNAECOLOGICAL MALIGNANCY

Shalu Kumari¹, Amita Maheshwari¹, Rohini Kulkarni¹, Sneha Raj¹, Kannan M², Biswajit Dash¹, Supriya Chopra³, Jaya Ghosh⁴. ¹Tata Memorial Hospital, Tata Memorial Centre (TMC), Homi Bhabha National Institute (HBNI), Gynec Oncology, Mumbai, India; ²Tata Memorial Hospital, Tata Memorial Centre (TMC), Homi Bhabha National Institute (HBNI), Biostatistics, Mumbai, India; ³Tata Memorial Hospital, Tata Memorial Centre (TMC), Homi Bhabha National Institute (HBNI), Radiation Oncology, Mumbai, India; ⁴Tata Memorial Hospital, Tata Memorial Centre (TMC), Homi Bhabha National Institute (HBNI), Medical Oncology, Mumbai, India

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Introduction: Vitamin D3 plays a key role in regulating calcium metabolism and regulates cell proliferation and differentiation. The present study aimed to evaluate prevalence of Vitamin D3 deficiency in women with gynecological malignancy.

Methods: Retrospective analysis of all consecutive newly diagnosed patients with gynecological cancer from August 2022 to December 2023. Data was retrieved from electronic medical records after obtaining Institutional Review Board approval. Patients were categorized based on their serum Vitamin-D3 level: sufficiency was defined as >30–40 ng/mL, insufficiency as 20–30 ng/mL, and deficiency as <20 ng/mL.

Results: Serum Vitamin D3 levels were available for 651 patients. 61.3% (399) had a deficiency, 20.3% (132) had insufficiency and a normal level was observed in only 18.4% (120) patients. Cervical cancer (42.7%) was the most common cancer followed by ovarian (41.9%) and uterine cancers (12%). Patients without Vitamin-D3 deficiency were significantly older by 4 years than those with deficiency, median age 56 vs. 52 years ($p < 0.001$). Hypertension was significantly associated with increased odds of Vitamin D3 deficiency (OR = 3.03, 95% CI: 1.68–5.44), while other comorbidities, including diabetes (OR = 1.93, 95% CI: 0.92–4.02) and multiple conditions (OR = 1.63, 95% CI: 0.92–2.87), showed non-significant trends. No significant association was found between cancer type & stage and Vitamin-D3 levels.

Conclusion/Implications: Vitamin-D3 deficiency/insufficiency was highly prevalent in Indian patients with gynaecological cancer and was significantly associated with hypertension and younger age ($p < 0.001$), which was independent of cancer type and stage. Routine measurement of serum Vitamin-D3 level and appropriate correction should be offered along with cancer-directed treatment.

Table 1. Demographic and clinical characteristic among the cohort

Baseline characteristic	Total Number of patients	Normal Vit-D3	Insufficiency/Deficiency Vit-D3
N (%)	651 (100%)	120 (18.4%)	531 (81.6%)
Menstrual status			
Pre-Menopausal	205 (31.5%)	27	178
Post Menopausal	446 (68.5%)	93	353
Age yrs			
Median (Range)	53 (16-79)	56 (26-75)	52 (16-79)
Cancer site			
Cervix	273 (41.9%)	52 (19.1%)	221 (80.9%)
Ovary	278 (42.7%)	46 (16.5%)	232 (83.5%)
Uterus	78 (12%)	20 (25.7%)	58 (74.3%)
Vulva + Vagina	15 (2.3%)	0 (0%)	15 (100%)
GTN	7 (1.1%)	2 (28.5%)	5 (71.4%)
STAGE			
Stage I	76 (11.7%)	18 (23.7%)	58 (76.3%)
Stage II	98 (15.1%)	17 (17.3%)	81 (82.7%)
Stage III	314 (48.2%)	53 (16.9%)	261 (83.1%)
Stage IV	163 (25%)	32 (19.6%)	131 (80.4%)

EP011 / #597

CYTOTOXIC EVALUATION OF A PERITONEAL CISPLATIN SLOW-RELEASE MEMBRANE FOR OVARIAN CANCER TREATMENT: AN ANIMAL MODEL

Marcelo Simonsen^{1,2}, Maria Katayama¹, Mara Alcântara³, Mara Junqueira¹, Fernando Aguiar¹, Ademair Lugão³, Leda Talib⁴, Maria Estevez-Diz⁵, Igor Marcondes De Andrade², Najla Tayfour², Eric Mayerhoff², Audrey Tsunoda^{6,7,8}, Marcelo Antonini², Lais Silva², Andressa Teixeira², Isabela Barboza², Michelle Samora⁹, Mariana Scaranti¹⁰, Tais De Oliveira², Paulo Laginha¹⁰, Marília Bertolazzi², Andrea Soares², Bruno Fernandes², Maria Figueira². ¹Instituto do Câncer do Estado de São Paulo - ICESP, São Paulo, Brazil; ²Hospital do Servidor Público Estadual de São Paulo, Gynecology, São Paulo, Brazil; ³Instituto de Pesquisas Energéticas e Nucleares - IPEN, São Paulo, Brazil; ⁴Instituto de Psiquiatria do Hospital das Clínicas de São Paulo, São Paulo, Brazil; ⁵Instituto do Câncer do Estado de São Paulo - ICESP, FMUSP, São Paulo, Brazil; ⁶Hospital Erasto Gaertner, Curitiba, Brazil; ⁷PUC-Paraná; HCor - São Paulo; Hospital Erasto Gaertner - Curitiba, Curitiba, Brazil; ⁸Pontifícia Universidade Católica do Paraná, Paraná, Brazil; ⁹Hospital do Coração - HCor, São Paulo, Brazil; ¹⁰Hospital 9 de Julho, São Paulo, Brazil

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Introduction: Platinum-based drugs remain the cornerstone of chemotherapy for ovarian cancer. While various forms of intracavitary chemotherapy offer potential clinical benefits, they are often associated with significant toxicity, which may limit the advantages of localized treatment. Alternative intraperitoneal delivery methods are needed to reduce systemic side effects.

Objective: To develop and evaluate a cisplatin-loaded membrane designed for sustained, slow drug release, with the goal of reducing toxicity and enhancing direct tumor exposure in murine models.

Methods: The membrane was synthesized via electrospinning of a solution containing acetic acid, dimethylformamide, bovine gelatin, and cisplatin. The highest concentration achieved without crystal formation was 5.3 mg/mL. In vitro drug release was evaluated over 20 days, followed by application in SKOV3 tumor cell cultures. In vivo studies were conducted in nude mice bearing SKOV3 xenografts, first as a pilot study and subsequently in a larger animal trial.

Results: Cisplatin release was more stable with increased membrane thickness compared to glutaraldehyde crosslinking. The membrane demonstrated effective tumor cell control in in vitro SKOV3 assays. However, in vivo, free cisplatin administered into the peritoneal cavity was more effective than the membrane in reducing tumor burden. Weight loss and animal toxicity profiles were not significant across all groups.

Conclusion/Implications: The membrane prototype showed promising in vitro results. However, further optimization of the release kinetics is needed to maintain therapeutic drug levels for more than 10 days in vivo.

EP012 / #908

COMBINED TARGETING OF NUCLEAR IMPORT AND EXPORT RECEPTORS RESULTS IN SYNERGISTIC INHIBITION OF CERVICAL CANCER CELLS.

Paul Nayim¹, Pauline Van Der Watt^{1,2}, Virna Leaner^{1,3}. ¹University of Cape Town, Division Of Medical Biochemistry And Structural Biology, Department Of Integrative Biomedical Sciences, Cape Town, South Africa; ²Institute of Infectious Disease and Molecular Medicine, University of Cape Town, Cape Town, South Africa; ³UCT/SAMRC Gynaecological Cancer Research Center (GCRC), Faculty of Health Sciences, University of Cape Town, Cape Town, South Africa

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Introduction: The nuclear transport receptors, Karyopherin Beta 1 (Kpnβ1) and Exportin 1 (Crm1), have previously been found to be overexpressed in cervical cancer. This study aimed to investigate the impact of concomitant inhibition of Kpnβ1 and Crm1 on cervical cancer cell biology.

Methods: Bioinformatic analyses were used to assess the relationship between Kpnβ1 and Crm1 expression in cervical cancer patient tissue and their association with cancer patient survival. Cultured cancer cell lines were treated with the small molecule inhibitors, Selinexor and INI-43 (for inhibition of Crm1 and Kpnβ1, respectively), and the Chou-Talalay method analysed the effect of their co-inhibition, while apoptosis assays confirmed the mode of cell death.

Results: A positive correlation was found between Kpnβ1 and Crm1 gene expression in cervical cancer patient tissue and, when combined, the high expression of Kpnβ1 and Crm1 associated with poor patient survival. Co-treatment of cervical, ovarian and uterine cancer cells with Selinexor and INI-43 resulted in synergistically enhanced cancer cell death, compared to treatment with either inhibitor alone, while non-cancer cells were less sensitive to treatment with both inhibitors. Combined treatment of cells also resulted in increased markers of apoptosis, including PARP-1 cleavage and activation of Caspase 3/7. Finally, it was found that co-treatment of cells with INI-43 and Selinexor resulted in decreased p65 transcriptional activity, and an inhibitor of NFκB, sodium salicylate, potentiated the combined effects of INI-43 and Selinexor on cancer cell viability.

Conclusion/Implications: Combined treatment of cervical cancer cells with nuclear import and export inhibitors has potential as an anticancer approach.

EP013 / #398

CLINICAL SIGNIFICANCE OF 99MTC-METHYLENE DI-PHOSPHONATE BONE IMAGING & MOLECULAR BIOLOGY IN THE DIAGNOSIS OF BREAST CANCER BONE METASTASES.

Dr. Karan Peepre. Mahatma Gandhi Medical College, Hospital & University of Medical Sciences & Technology, Jaipur, Nuclear Medicine, Jaipur, India

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Introduction: Clinical research and medical therapies arising from molecular biology and the use of molecular cell biology approaches in medicine is now called molecular medicine. Biological molecules are predominantly three-dimensional and structural, it must inquire into genesis and function. Breast Cancer is most prone to metastasize to long bones. Present scenario involves 99mTechnetium methylene di-phosphonate (99mTc MDP) bone scintigraphy method of choice for the detection of bone metastases. To help diagnose pathology of the skeletal system, patients are injected with radiopharmaceuticals composed of Technetium-99m and a bone-seeking molecule such as analogs of calcium, and diagnosis is made.

Methods: All patients underwent whole-body bone planar scintigraphy in the anterior and posterior positions 3 hours after injection. A dose of 22 to 30 mCi of 99mTc-MDP was injected IV, entire skeleton was taken under the gamma camera imaging machine.

Results: Total 53 females, 25- 72 years were accounted for the study. Out of which 50 females was histopathologically diagnosed as cancer breast. They have been referred to nuclear medicine with the history of lump in breast with pain in joints. On visual analysis there was positive scan findings (bone metastases) in 19 patients (35.84 %) and negative scan findings (normal bone scan) in 34 patients (66.6%).

Conclusion/Implications: In this series of breast cancer patients 99mTc-MDP scan proves highly sensitive in measuring the extent of bone metastasis in breast cancer. It elucidates, non-invasively, lesion characteristics and indicative for prognosis and response to chemotherapy and hormonal treatment.

EP014 / #424

DETECTION OF BIS(2-ETHYLHEXYL) PHTHALATE IN THE VAGINA AS A MEASUREMENT OF EXPOSURE IN PATIENTS WITH ENDOMETRIAL CANCER

Ana Rosario Santos^{1,2}, Matthew Schlumbrecht¹, Harun Roshid², Gregory O'Connor², Sapna Deo², Sylvia Daunert². ¹University of Miami Miller School of Medicine, Gynecologic Oncology Division, Miami, United States of America; ²University of Miami Miller School of Medicine, Biochemistry And Molecular Biology, Miami, United States of America

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Introduction: The incidence of endometrial cancer (EC) is increasing worldwide. To date, few studies have investigated the role of environmental exposures on risk of EC. Candidate molecules for such studies include phthalates, which are endocrine-disrupting chemicals (EDCs) from the plasticizer industry. Evidence suggests that EDCs may play a role in EC development through alterations in estrogen signaling pathways and the local immune microenvironment. No studies have investigated their presence in the vagina as a measurement of exposure. Our aim was to quantify bis(2-ethylhexyl) phthalate (DEHP), a probable carcinogen, in the vagina of EC patients compared to a benign control.

Methods: Vaginal swabs were collected at time of hysterectomy for both EC and benign disease; five patients were used for this pilot investigation. Phthalate extraction was performed using acetonitrile as an organic solvent, facilitating the detection of DHEP using ultra-performance liquid chromatography-tandem mass spectrometry (UPLC-MS/MS). A linear calibration curve for DEHP was optimized for a detection range of 0.01 ng/mL to 200 ng/mL, achieving an R² coefficient greater than 0.99.

Results: DEHP was identified in all four patients with cancer and one benign control (adenomyosis). The average vaginal DEHP concentration ranged from 2.7124 ng/mL - 46.2877 ng/mL (Table 1). DEHP concentration was higher in all EC specimens compared to benign control.

Table 1. DEHP concentrations in vaginal swab extractions by UPLC-MS/MS

Histology	DHEP concentration (ng/mL)
High-grade serous endometrial carcinoma	38.6919
Endometrioid FIGO grade I adenocarcinoma	46.2877
Endometrioid FIGO grade I adenocarcinoma	10.2013
Endometrioid FIGO grade I adenocarcinoma	9.0321
Adenomyosis	2.7124