HYPERMETHYLATION FOR CERVICAL CANCER SCREENING AMONG HIV-POSITIVE WOMEN IN SOUTH AFRICAN
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Objectives We investigated the role of molecular markers in cervical cancer screening for South African women living with HIV (WLHIV).

Methods South African WLHIV underwent cervical screening and colposcopy-directed biopsy with molecular screening. Data analysis was done on DNA isolated from cervical scrapes. Diagnostic performance of cytology and HPV tests alone and combined with FAM19A4/miR124–2 hypermethylation was performed.

Results 285 women were included in the analyses. Cytology provided the highest specificity (91.6%), but lowest sensitivity (59.3%), HPV (high-risk) provided the highest sensitivity (83.1%), but lowest specificity (66.4%). Combining cytology with methylation did not improve the performance of cytology alone, but triage of HPV (high-risk) with methylation, increased specificity (76.1%) while maintaining an acceptable sensitivity (72.9%). Similar performance was observed for HPV (16/18) with methylation triage (sensitivity 79.7%, specificity 74.8%). Number referred per CIN 3+ was lowest for HPV (16/18) with methylation triage (sensitivity 79.7%, specificity 2.2). Patients with LNR ≤ 0.03 had a survival of 50 months vs. 27 months in patients with LNR > 0.03.

Conclusions Huge efforts including extensive cytoreductive surgeries are being performed at institutions in developing countries in order to improve survival and lower recurrence in ovarian cancer patients.

LEBANESE EXPERIENCE WITH CYTOREDUCTIVE SURGERY IN OVARIAN CANCER: A SINGLE INSTITUTION SERIES
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Objectives To review the surgical outcomes of cytoreductive surgery for ovarian cancer in a single institution.

Methods We reviewed all patients with ovarian cancer who received a cytoreductive surgery between January 2005 and December 2018 at Hôtel-Dieu de France University Hospital, Lebanon.

Results 161 patients were included. Mean age at surgery was 54 years (range 16 – 83 years). Cytoreductive surgery was done in four settings: upfront surgery (40%), interval surgery post neoadjuvant chemotherapy (42%), post recurrence (7%), post incomplete primary surgery (11%). 67% of operated patients were in stage III. Surgical resection included bowel resection (48%), diaphragmatic peritoneal resection (25%) and splenectomy (15%). 89% of patients received a pelvic and para-aortic lymphadenectomy. Node involvement was noted in 48% of cases. No recurrence was seen in 56% of cases and the mean interval of recurrence was estimated at 21 months with 78% of recurrences occurring after 12 months from surgery. Overall survival was estimated at 40 months (range 2 – 165 months). No impact on survival was detected whether the patient benefited from an upfront surgery or an interval one post neoadjuvant chemotherapy: 36 months vs 30 months respectively, (p= 0.39). Better survival was encountered when only one lymph node was involved (85 months vs 42 months, p=0.037). Patients with LNR ≤ 0.03 had a survival of 50 months vs. 27 months in patients with LNR > 0.03.

Conclusions Wnt/β-catenin signaling is frequently dysregulated in gynecologic malignancies. CTNNB1, APC and RNF43 mutations cause pathway activation; CTNNB1 stabilizing mutations lead to elevated DKK1 expression which promotes an immune suppressive tumor microenvironment. Neutralization by DKN-01 (D), a mAb against DKK1, is being tested in a phase 2 basket study.

Methods Eligibility included recurrent endometrial cancer (EC) or platinum resistant/refractory ovarian cancer (OC) enriched (~50%) for Wnt signaling-related genetic alterations. Subgroup analysis was done in pts with genetic alterations associated with activation of Wnt/β-catenin signaling (CTNNB1, APC or RNF43). Pts were assigned (MD discretion) to receive D (300 mg on Days 1 & 15) or D + paclitaxel (P) (80 mg/m2 on Days 1, 8 and 15) of a 28-day cycle. Primary endpoint is: Pathway mutations respond better to DKN-01, a DKK1 inhibitor.

PATIENTS (PTS) WITH RECURRENT GYNECOLOGIC CANCER WHOSE TUMORS HAVE ACTIVATING WNT PATHWAY MUTATIONS RESPOND BETTER TO DKN-01, A DICKKOPF-1 (DKK1) INHIBITOR
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Objectives Wnt/β-catenin signaling is frequently dysregulated in gynecologic malignancies. CTNNB1, APC and RNF43 mutations cause pathway activation; CTNNB1 stabilizing mutations lead to elevated DKK1 expression which promotes an immune suppressive tumor microenvironment. Neutralization by DKN-01 (D), a mAb against DKK1, is being tested in a phase 2 basket study.
IGCS19-0049

CERVICAL PRE-CANCER VS INVASIVE CANCER: MOLECULAR DIFFERENTIATION WITH POTENTIAL OF IMPROVING CERVICAL CANCER SCREENING WORLDWIDE

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ORR; exploratory endpoints: DKK1 expression (serum/plasma/tumor), tumor genetics, infiltrating immune cells, and β-catenin IHC.

Results 80 pts are enrolled: D (n=33, 19 EC, 14 OC); D + P (n=47; 28 EC, 19 OC); 18 pts with CTNNB1 (n=13), APC (n=2), RNF43 (n=2), or CTNNB1 + RNF43 (n=1). 54 pts evaluable for response (table 1). D and D + P were safe and well tolerated with no additive toxicities. The trial is ongoing; updated safety, efficacy and correlative work are pending.

Conclusions D and D + P have activity in pts with recurrent gyn cancers; the role of Wnt/β-catenin pathway activation as a potential biomarker for response is currently under study. Clinical trial information: NCT03395080.

Conclusions The S5 methylation classifier may be useful in cervical screening programs for identifying progressive pre-cancers in women. Although the separation was very good, there is room for improvement by addition of new markers derived from our ongoing NGS multi-omics study.

IGCS19-0225

IGCS GYNECOLOGY ONCOLOGY GLOBAL CURRICULUM AND MENTORSHIP PROGRAM IN MOZAMBIQUE: CHALLENGES AND RESULTS OF AN OVERSEAS SURGICAL TRAINING PROGRAM

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Objectives To describe the implementation of the IGCS Gynecologic Oncology Global Curriculum and Mentorship Program (Global Curriculum) in Mozambique.

Methods The Global Curriculum is a training program for regions that do not have formal training in Gynecologic Oncology. The Mozambique program is a collaboration between Maputo Central Hospital, five institutions in Brazil and MD Anderson Cancer Center. In January 2016, three Obstetrician-Gynecologists were selected as the Global Curriculum fellows. They follow an on-line curriculum, receive quarterly visits from international mentors, participate in monthly tumor boards using Project ECHO and enter case logs into the REDcap system.

Results To date, there have been 9 visits to Mozambique. Each visit consists of didactic lectures, surgical training, multidisciplinary care and the management of preivansive desease. Between visits, monthly videoconferences are held to discuss patient cases. A total of 91 surgeries have been performed, including 45 radical hysterectomies, 11 cold knife conizations and 14 radical vulvectomy. Six colposcopy and LEEP courses were held with 202 attendees from all provinces of the country, 174 colposcopies and 35 LEEPs performed. In August 2018, a patient underwent radical hysterectomy and it was the first time this procedure was performed exclusively by Mozambican surgeons.

Conclusions The IGCS model of surgical training is feasible and has already shown good results for the oncology patients and fellows in Mozambique.