

Abstract 76 Table 1

	Evaluable N	PR N	SD N	PD N	DCR N (%)
D	19	2	7	10	9 (47.4)
EC	10	2	3	5	5 (50.0)
OC	9	0	4	5	4 (44.4)
CTNNB1, APC, RNF43	5	1	3	1	4 (80.0)
D + P	35	1	21	13	22 (62.9)
EC	18	1	9	8	10 (55.5)
OC	17	0	12	5	12 (70.6)
CTNNB1, APC, RNF43	9	1	4	4	5 (55.5)

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.

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

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Objectives The S5 DNA-methylation classifier, based on target CpG sites of the human gene *EPB41L3*, and viral late gene regions of HPV-16,18,31 and 33 (Lorincz A *et al.*, 2016) has demonstrated better performance for detection of CIN2/3-women than either HPV16/18 genotyping, cytology or combination. We tested the performance of S5 in detecting invasive cancers versus pre-cancers and quantified the degree of separation between normal/CIN1, CIN2/3 and invasive cancer S5 scores.

Methods Methylation status of the S5-CpGs was tested in DNA extracted from exfoliated cervical cell from the UK (n=138), Spain (n=100), Colombia (n=96), Philippines (n=50), Georgia (n=42) and Ethiopia (n=79). Samples were histologically defined as negative/CIN1, CIN2/3 and invasive cancer. DNA-bisulfite conversion was carried out and followed by pyrosequencing for the 6 components of S5. Average methylation was calculated for each marker to define the S5 score.

Results Methylation at all sites increased proportionally with disease severity showing a Cuzick-trend of $z=9.2933$ ($p<2.2\times 10^{-16}$). The separation of normal/CIN1 from CIN2/3 and from cancer was highly-significant (Mann-Whitney, all $p<0.0001$). S5 also showed highly-significant difference

between CIN2/3 and invasive cancer from matched cohorts: UK ($p<0.003$), Spain ($p<0.0001$) and Colombia ($p<0.003$). ROC-curves were used to assess the diagnostic potential of S5 in differentiating cancers from CIN2/3. The AUC was 0.86 (CI 95%: 0.7965 to 0.9131, $p<0.0001$) with a sensitivity of 79.8% and a specificity of 83.1%, based on a cut-off at highest Youden J-index.

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.

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78 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, multi-disciplinary care and the management of pre-invasive disease. 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 vulvectomies. 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.