Future work

- Finalise EWAS model, explore HPV effect on methylation
- Validate EWAS findings in our lab in a separate cohort of women with CIN and cancer
- Explore ability of epigenetic markers to predict progression or regression of CIN2
- Umbrella review of environmental and behavioural risk factors for cervical cancer with mendelian randomisation

Thankyou to

All the patients who participated in our studies

And for significant contributions to this work:

Ilkka Kalliala
Maria Paraskeva
Barbara Bodinier
Areti Veroniki
Nahal Masrour
Kostas Lathouras
Verena Zuber
Dragana Vuckovic
Maria Nasioutziki
Iriana Dougeraki
Nuntawat Chaitrakulthong
Menelaos Tzafettas
Anita Mitra
Phil Bennett
Marjo-Ritta Jarvelin
Konstantinos Tsilidis
Marc Chadeau-Hyam
James Flanagan
Maria Kyrgiou

Funders

Institute of Reproductive and
Developmental Biology

School of Public Health

FINNGEN

Abstract 200 Figure 1

Methylation signatures of cervical cancer genes are promising for future diagnostic and prognostic tools.

218

WORSE PROGNOSIS OF HUMAN PAPILLOMAVIRUS NEGATIVE COMPARED TO HUMAN PAPILLOMAVIRUS POSITIVE CERVICAL CANCER

¹N Kugelman*, ¹E Siegler, ¹L Mackuli, ¹O Lavie, ¹M Schmidt, ²P Shaked Mishan, ¹Y Segev.
¹Carmel Medical Center, Obstetrics and Gynecology, Rappaport Faculty of Medicine,
Technion-Israel Institute of Technology, Haifa, Israel; ²Carmel Medical Center, Clinical
Serology and Virology Laboratory, Haifa, Israel

10.1136/ijgc-2021-ESGO.18

Introduction/Background* To evaluate the prevalence and prognosis of human papillomavirus (HPV)-negative cervical cancer (CC), and compare these to data for HPV-positive CC.

Methodology This retrospective cohort study compared between HPV-negative CC and HPV-positive CC patients. Primary endpoints were recurrence-free survival, disease-free survival, and overall survival. Secondary endpoints were demographic and clinical variables including histological diagnosis, stage, and treatment.

Result(s)* Of 233 women with CC, 18 (8%) were HPV negative. During a median follow up of 45 months, 33 (14%) recurrences and 41 (18%) deaths were observed. Eleven (61%) of the 18 women who were HPV negative and 41 (19%) of the 215 who were HPV positive had only adenocarcinoma ($P<0.001$). In a multivariate logistic regression analysis, adenocarcinoma histology at diagnosis ($P=0.010$) and primary treatment with chemotherapy or radiotherapy ($P=0.011$) remained statistically significant for recurrence. The factors associated with lower survival were advanced age ($P=0.008$), higher stage at diagnosis ($P<0.001$) and HPV

Abstract 218 Table 1 Multivariate analysis for overall survival. Recurrence-free survival, and disease-free survival of cervical cancer patients

	Hazard Ratio (CI 95%)	P-value
5-year mortality		
HPV negative	2.19 (0.99-5.01)	0.062
Advanced age	1.09 (1.01-1.05)	0.008
Higher stage at diagnosis (183-48)	7.27 (2.52-20.99)	<0.001
5-year recurrence		
HPV negative	1.75 (0.66-4.65)	0.261
Adenocarcinoma	2.77 (1.28-6.03)	0.010
Chemo/Radiation as primary treatment	3.06 (1.29-7.29)	0.011
Advanced age	1.023 (0.99-1.05)	0.084
Disease-free survival		
HPV negative	1.57 (0.73-3.39)	0.246
Advanced age	1.03 (1.01-1.05)	0.003
Chemo/Radiation as primary treatment	3.79 (1.89-7.62)	<0.001
Adenocarcinoma	1.65 (0.88-3.12)	0.120

Abstract 218 Figure 1 Kaplan Meier curve of overall survival, comparing women with HPV-negative and HPV-positive cervical cancer

negativity ($P=0.062$). Median overall survival for HPV-positive CC was not reached, compared to 24 months for HPV-negative CC. Kaplan-Meier curves showed lower rates of overall survival ($P=0.011$), recurrence-free survival ($P=0.005$) and disease-free survival ($P=0.008$) for women with HPV-negative compared to HPV-positive CC.

Conclusion* The relatively poor prognosis of HPV-negative CC is important in light of its relatively high prevalence, which could increase proportionally to HPV-positive CC due to increased HPV screening and vaccination. Further studies are needed to confirm if HPV status is truly an independent prognostic factor in CC.

226 CLEARANCE OF HPV AFTER CONIZATION OF CERVICAL CANCER AND ADENOCARCINOMA IN SITU CORRELATES WITH ABSENCE OF CANCER

¹N Kugelman*, ¹E Siegler, ¹Y Goldberg, ²Y Siegler, ³P Shaked Mishan, ⁴S Mazareb, ¹L Mackuli, ⁴E Sabo, ²O Lavie, ²Y Segev. ¹Carmel Medical Center, Obstetrics and Gynecology, Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel; ²Rambam Health Care Campus, Obstetrics and Gynecology, Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel; ³Carmel Medical Center, Clinical Serology and Virology Laboratory, Haifa, Israel; ⁴Carmel Medical Center, Pathology, Haifa, Israel

10.1136/ijgc-2021-ESGO.19

Introduction/Background* About 40% of CC are in women under age 40 years, for whom fertility-sparing treatment might be very important and should always be considered. More than half the patients who undergo radical surgery (trachelectomy or hysterectomy) have no remnant tumor in the final pathology specimen. HPV clearance is a test of cure after conisation, but it is not a test of cure in CC. Our objective was to assess correlation of clearance of high-risk human papillomavirus (HR-HPV) after large loop excision of the transformation zone (LLETZ) with absence of residual disease, in women diagnosed with cervical cancer (CC) and Adenocarcinoma in Situ (AIS).

Methodology Data was collected from 92 women diagnosed with CC and AIS who were positive to High-Risk HPV (HR-HPV), and had a repeat cervical HPV test 3-12 weeks post-LLETZ, and before final surgical treatment. We compared characteristics of women with negative and positive HR-HPV post-LLETZ.

Result(s)* The pathological results of women who were HR-HPV negative ($n=40$) compared to HR-HPV positive ($n=52$) at the post-LLETZ follow-up visit included a significantly higher incidence of AIS: 14 (35%) vs 5 (9.6%) ($p<0.006$). In the negative HR-HPV post-LLETZ group, 36 (90%) had normal histology and only 2 (5%) had cancer in the final histological specimen. Among women who underwent radical hysterectomy/trachelectomy after LLETZ, a normal final histology was observed in 75% and 9% of those who were HR-HPV negative and HR-HPV positive, respectively ($p<0.0005$). The negative predictive value for residual cancer, with clearance of HR-HPV after LLETZ was 95%.

Conclusion* Clearance of HR-HPV from the cervix a short time after LLETZ has a high correlation with the absence of residual cancer in the final outcome, either in the pathology or the follow up. Testing for HR-HPV a short time after LLETZ might serve as a parameter for risk assessment.

245 THE SIGNIFICANCE OF SURGICAL ASSESSMENT IN ONCOLOGICAL OUTCOMES AFTER RADICAL HYSTERECTOMY FOR EARLY-STAGE CERVICAL CANCER. A MULTICENTER STUDY

¹S Fernandez-Gonzalez*, ²M Barahona, ³A Gil-Moreno, ³NR Gómez-Hidalgo, ⁴B Diaz-Feijoo, ⁵P Coronado, ⁵V González, ⁵A Casajuana, ⁶JM Silvan, ⁶L Melero, ⁶MA Martinez, ⁷J Hilario de la Rosa, ⁷I Lobo, ⁷E Beiro, ⁸J Frias-Gomez, ⁸Y Benavente, ²C Ortega, ⁹E Martinez, ²L Marti, ²J Ponce. ¹University Hospital of Bellvitge (IDIBELL), Gynecology, L'Hospitalet de Llobregat, Spain; ²University Hospital of Bellvitge (IDIBELL), Gynecology, L'Hospitalet de Llobregat (Barcelona), Spain; ³Hospital Universitari Vall d'Hebron, Department of Gynecologic Oncology, Barcelona; ⁴Hospital Clínic de Barcelona, Gynecology, Barcelona, Spain; ⁵Hospital Clínic San Carlos, Instituto de Salud de la Mujer, Madrid, Spain; ⁶Hospital Universitario Virgen del Rocío, Gynecology, Sevilla, Spain; ⁷Hospital Universitario de Basurto, Gynecology, Bilbao, Spain; ⁸Catalan Institute of Oncology (IDIBELL), Cancer Epidemiology Research Programme, L'Hospitalet de Llobregat, Spain; ⁹University Hospital of Bellvitge (IDIBELL), Nursery, L'Hospitalet de Llobregat (Barcelona), Spain, Spain

10.1136/ijgc-2021-ESGO.20

Introduction/Background* Patients with early-stage cervical cancer [CC] had worse prognosis when operated by minimal invasive surgery according to LACC trial. Different hypothesis were suggested such as the intrauterine manipulator, the CO₂ or the lack of protective manoeuvre. However, the effect of surgical expertise among patients who underwent radical hysterectomy by the same approach has not been evaluated.