Molecular alterations predictive of outcome in early staged cervical cancer: A translational investigation from the Senticol III trial

1Maryame El Gani*, 2Sabrina Ibadoune, 3Zakhia El Beaino, 4Sophie Vacher, 5Alexandre Degrieux, 6Emmanuelle Jeanmot, 7Julien Masliah-Flanchon, 8Anne Vincent-Salomon, 9Gwenaël Ferron, 10François Goffier, 11Eris Lambaudie, 12Fabrice Narducci, 13Cécile Loaec, 14Jennifer Uzan, 15Ferdié Chad, 16Marie Plante, 17Maud Kamal, 18Fabrice Lecuru, 19Ivan Bilche. Department of Gynecological Oncology and breast surgery, Institut Curie Paris, Paris, France; 2Department of Genetics, Institut Curie, Paris, France, Paris, France; 3Department of Pathology, Hôpital Tenon AP-HP, Paris, France, Paris, France; 4Department of Genetics, Institut Curie, Paris, France; 5Biological Resources Center, Institut Curie, Paris, France, France; 6Department of Genetics and Department of Pathology, Institut Curie, Paris, France; 7Department of Pathology, Institut Curie, Paris, France, France; 8Department of Surgical Oncology, IUCT-Institut Claudius Regaud, Toulouse, France; 9Dept of Gynecological and Oncological Surgery, CHU Lyon Sud – Hospices Civils de Lyon, Lyon, France; 10Department of Gynecologic Oncology, Institut Pauli Calmettes, Marseille, France; 11Department of Gynecologic Oncology, CLLC Centre Oscar Lamberit, Lille, France; 12Department of Gynecologic Oncology, Institut de Cancérologie de l’Ouest Centre René Gauducheau, Saint-Herblain, France; 13Department of Obstetrics and Gynecology, Centre Hospitaller Intercommunal de Créteil, Créteil, France; 14Dept of Gynecological and Oncological Surgery, Institut de Cancérologie de Lorraine, Université de Lorraine, Vandœuvre-Les-Nancy, France; 15Department of Gynecologic Oncology, CHU de Québec, Université Laval, Québec, Canada; 16Department of Gynecologic Oncology, CHUV – Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland; 17Drug Development and Innovation Department, Institut Curie., Paris, France; 18Department of Gynecological Oncology and breast surgery, Paris, France; 19Department of Genetics, Institut Curie., Paris, France.

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Introduction/Background Despite of a well managed surgery and good histological and clinical features, some patients relapse after the treatment of early stage cervical cancer. The comprehensive genetic and molecular characteristics of malignant cervical tumours were described by The Cancer Genome Atlas Research Network. However, the TCGA data only published sequencing results with few clinical and histological data. Yet, the literature remains scarce about genetic alterations and outcome correlation in early stage cervical cancer.

Our translational study use a pan-genomic approach to evaluate recurrent genetic alterations seen in early cervical cancer patients. We aim to evaluate the correlation between molecular findings and clinical outcome and to find new prognostic biomarkers in early cervical cancer.

Methodology We included the first 150 patients randomized in the Senticol III trial. This large multicentric, prospective, randomized, and international ‘validation study’ tries to validate sentinel node biopsy as nodal staging of early cervical cancers (stage Ia – Ia1).

Cervical tumor slides were analyzed and stratified based on well-established histological criteria (SDISL criteria). The immune microenvironment characteristics including TIL’s in filtration and PD1L1 CPS score were assessed. We made HPV detection and typing by PCR of the tumor samples. We performed DNA and RNA extractions from the FFPE tumor specimens. Using the dedicated gene panel developed by our team, we analyzed 571 genes commonly altered in cancer. We performed high throughput RNA sequencing to establish the gene expression profile of each tumor and its associated stroma.

The genomic and transcriptomic analysis assessed the tumor mutational load, the most frequently altered genes and their expression. The biostatistical analyses will correlate molecular alterations, histopathological and clinical features, with patient outcome. The different parameters will be first analyzed independently (univariate analysis) and then in a multi-parametric manner (logistic regression).

Results The malignant potential of these concurrent multiple infections with HR-HPVs, including HR-HPV 16, has been known as the most important carcinogen in uterine cervical carcinoma. Concurrent multiple infections with HR-HPV are prevalent in young women. However, there is limited evidence on the malignant potential of these concurrent multiple infections.

Methodology This study included women aged below 36 years undergone cervical conization from 2012 to 2023. They underwent an HPV test by cervical swab within 12 months prior to the surgery. The HPV test was performed using DNA microarray or real-time polymerase chain reaction. They were divided into two groups: one with a single infection with HR-HPV 16 and the other with concurrent multiple infections with HR-HPVs, including HR-HPV 16. Additionally, they were categorized into two groups based on the pathologic result of conization: one was HSIL+, including high-grade squamous intraepithelial lesion (HSIL), carcinoma in situ (CIS), invasive carcinoma, and the other was CIS+, including HSIL, CIS, invasive carcinoma. The ratio of HSIL+ or CIS+ between the groups was analyzed using logistic regression. All statistical analyses were conducted using SPSS version 26 (IBM Corp., Armonk, NY, USA).

Results Of the included patients, 76 were found to be infected with HPV 16. The single-infection group consisted of 31 (40.8%), whereas the group with concurrent multiple infections consisted of 45 (59.2%). In the logistic regression used to compare the malignant potential between the groups, no significant difference was observed. For HSIL+, the odds ratio was 1.032 (95% CI = 0.256–4.169, P = 0.964) between the single-infection and concurrent multiple infection groups, whereas for CIS+, it was 0.583 (95% CI = 0.238–1.427, P = 0.383).

Conclusion The malignant potential was not significantly different between concurrent multiple infections with HR-HPVs, including HPV 16, and a single infection with HR-HPV 16 in young Korean women. However, this result should be validated in a larger cohort.

Disclosures No disclosures declared.