AISP - 37th National Congress. **Bologna, Italy. September 19-21, 2013**

EZH2 Expression and Polymorphisms in Advanced Pancreatic Cancer

Niccola Funel[1], Mina Maftouh[2], Pinuccia Faviana[1], Amir Avan[2], Luca E Pollina[1], Sara Caponi[1], Michele Milella[3], Maurizio Cantore[4], Paola Pacetti[4], Andrea Mambrini[4], Enrico Vasile[1], Michele Reni[5], Ugo Boggi[1], Daniela Campani[1], Elisa Giovannetti[2]

[1]Department of Pathology, Surgery and Oncology, University of Pisa. Pisa, Italy. [2]VU University Medical Center. Amsterdam, The Netherlands. [3]Regina Elena National Cancer Institute. Rome, Italy. [4]Carrara Civic Hospital. Carrara, Italy. [5]San Raffaele Scientific Institute. Milan, Italy

Context Most pancreatic ductal adenocarcinoma (PDAC) patients present with advanced disease (i.e., locally-advanced or metastatic) at diagnosis, and identification of prognostic biomarkers is essential to improve their clinical management. Enhancer of Zeste Homolog-2 (EZH2) plays an essential role in cancer-stem-cell self-renewal through methylation of histone-H3. In radically-resected patients, nuclear accumulation of EZH2 was associated with increased invasiveness [1] and poor prognosis. Still, no data are available on the prognostic role of EZH2 in the subset of advanced PDACs. **Objective** This is the first study aimed at evaluating EZH2 mRNA and protein expression in locally-advanced or metastatic PDACs, that we enriched for tumor cell content by laser-microdissection. Furthermore, since (1) recent studies suggested a role for candidate polymorphisms of EZH2 in lung cancer risk and colorectal cancer prognosis, and (2) polymorphisms can be assessed with a simple test in blood samples, we evaluated the correlation of these polymorphisms with EZH2 expression as well as with outcome in two larger cohorts of patients. **Methods** EZH2 expression was evaluated by quantitative RT-PCR and immunohistochemistry in 32 and 20 specimens, respectively, while polymorphisms (rs6958683 and rs3757441) were studied also in blood samples from 2 additional cohorts of patients treated with gemcitabine monotherapy (n=93) or polychemotherapeutic regimens (n=247). **Results** EZH2 mRNA and protein expression correlated with survival (median overall survival of 6.7 months, 95% CI: 5.3-8.0, compared with 9.4 months, 95% CI: 1.6-17.2, in patients with low expression levels) and with the rs6958683 polymorphism, but this polymorphism was not associated with survival in our larger cohorts. **Conclusion** Our results showed that EZH2 expression correlated with survival and with the rs6958683 polymorphism in the first cohort of patients. However, this polymorphism was not associated with overall survival in the larger cohorts. Future efforts should evaluate other mechanisms in the triggering of PDAC by EZH2, as well as alternative prognostic markers for advanced PDAC.

Reference

1. Avan A, Crea F, Paolicchi E, Funel N, Galvani E, Marquez VE, et al. Molecular mechanisms involved in the synergistic interaction of the EZH2 inhibitor 3-deazaneplanocin A with gemcitabine in pancreatic cancer cells. Mol Cancer Ther 2012; 11:1735-46. [PMID: 22622284]