AB076. P048. Microsatellite instability and tumor volume inversely affect early progression free survival in adjuvant setting of patients with pancreatic ductal adenocarcinoma: lights and shadows of molecular pathology and immunotherapy

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Background: Pancreatic ductal adenocarcinoma (PDAC) may present microsatellite instability (MSI), phenotype related to a damage of DNA mismatch repair (MMR) system. The MSI-driven cancer pathway leads to the synthesis of aberrant and potentially immunogenic neo-antigens by the tumor cells. Immunotherapy with ICK inhibitors has recently constituted a source of personalized treatment for MSI cancer patients and support the evaluation of MSI phenotype in PDAC. The aim of this study is to evaluate MSI in PDAC patients presenting metastatic pathology after pancreatic resection featuring first line of chemotherapy in order to evaluate a possible immunotherapy treatment.

Methods: Ten patients affected by metastatic PDAC after surgical resection and adjuvant chemotherapy with curative intent were selected for MSI analyses. Immunohistochemistry (IHC) evaluations for genes MLH1, MSH2, MSH6 and PMS2 were performed. We assessed MSI when at the least 30% of selected markers lost their protein expression. Pathological data of primary tumor were assessed consulting VIII edition of TNM and the size of tumor was evaluated as volume (cm^3). Clinical data, progression free survival (PFS) and overall survival (OS) were obtained by Long-Rank tests.

Results: The mean follow-up was 19.02 months and the living patients were 70% (7/10). The median PFS and OS were 7.51 and 23.02 months, respectively. All patients showed a microsatellite stability, in which no alteration of protein expression in MMR system was found. Indeed, nobody was treated with immunotherapy. We identified 2 different groups (5 patients each), based on their early (E) or late (L) metastatic pathology (less or more 6 months after surgery), respectively. Furthermore, we found a significant difference in terms of PFS between these 2 groups (E *vs.* L; 2.20 *vs.* 14.63; HR =4.644; 95% CI, 3.982–103.200; P=0.0018). Nevertheless, we found significant differences comparing E *vs.* L group in terms of mean tumor score (2.780 *vs.* 1.870; P=0.0067) and volume (88.68 *vs.* 8.30; P=0.0068). No significant difference in term of OS were observed.

Conclusions: Our results confirmed that MMR/MSI alterations are very rare or absent in PDAC patients. This fact represents a limit in order to submit the PDAC patients to immunotherapy clinical trials. It's not still clear whether MSI pathways might be involved in early metastatic process of PDAC. Nevertheless, we showed that both tumor scoring and volume could play a pivotal role in early recurrence of pathology.

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