65P Potentially actionable mutations in intrahepatic cholangiocarcinoma

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Background: Intrahepatic cholangiocarcinoma (iCCA) is a liver neoplasm with few treatment options and a dismal prognosis. To date, the only curative option remains the surgery. New insights concerning its molecular pathogenesis and genetic heterogeneity are recently coming to light and are promising to widen the treatment landscape.

Methods: We evaluated data of the first 39 patients with iCCA included in the "Next Generation Sequencing in Intrahepatic Cholangiocarcinoma" study (EtherBil study, NCT02184871) from May 2014 to Dec 2017. For each patient enrolled, we performed whole exome sequencing ("WES)" on fresh frozen tumor tissue and peripheral blood DNA. All variants that were unique in the tumor sample were called as somatic. We used OncoKB (http://oncokb.org/) to define the clinical actionability of the somatic mutation identified (Chakravarty D. et al. JCO Precision Oncology 2017).

Results: A total of 33 actionable/potentially actionable mutations were identified in 17 genes. IDH1 (5/39, 12.8%), FGFR2 (4/39, 10.2%), IDH2 (3/39, 7.6%), KRAS (3/39, 7.6%), PIK3CA (3/39, 7.6%), NF1 (3/39, 7.6%) were the genes with the higher frequency of actionable/potentially actionable mutations. Remarkably, 20 out of 39 patients (51.2%) harbored at least one potentially actionable mutation. Furthermore, 2 out of 39 tumors were found to be ultra-hypermutated hypermutated ($\geq$100 Mut/Mb). The MSI-H/MMRd phenotype in the latter was confirmed by PCR and MLH1, PMS2, MSH2, and MSH6IHC immunohistochemistry.

Conclusions: Given the limited armory currently available in advanced unresectable iCCA patients, these data can be helpful to consolidate new understanding aimed at opening up future treatment options. Finally, we report the data of MSI-H/MMRd prevalence in our iCCA series having regard to the new insight on the immunotherapy in this subgroup of patients.

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