O-5 Frequency of minimal residual disease as measured by ctDNA in mismatch repair deficient tumors following curative resection

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Background: Mismatch repair deficient (MMRd) tumors are highly sensitive to checkpoint blockade (CPB) in patients with metastatic disease, regardless of tumor type. However, the efficacy of CPB in the adjuvant setting is unknown, especially since MMRd is considered a favorable biomarker for most resected tumor types. Circulating tumor DNA (ctDNA) could be used to screen for patients at high risk for recurrence following surgery or adjuvant chemotherapy, and identify patients (pts) that would most benefit from CPB.

Methods: To assess the frequency of ctDNA in the resected MMRd population, we prospectively screened pts with MMRd tumors who completed standard perioperative chemotherapy and surgery (NCT03832569). DNA from resected tumors and matched postoperative plasma was sequenced for the presence of somatic mutations. Patients were considered to have minimal residual disease (MRD) when mutations were identified in tumor and found to be identical to those in matched plasma DNA. Somatic tissue mutations were assessed using MSK-IMPACT and ctDNA was assessed using FoundationOne, Guardant360 or MSK-ACCESS.

Results: A total of 86 pts were screened for the presence of MRD. These represented 7 tumor types with colorectal (63%), endometrial (16%) and esophagogastric (13%) being the most common. The majority of pts were stage III (49%). MRD was detected in 18% of cases (14 of 79). Among the MRD-negative group (n=62), only one pt developed disease recurrence. Three samples failed ctDNA analysis for technical reasons.

Conclusions: MRD was identified in 18% of resected MMRd tumors using ctDNA analysis, suggesting this to be a feasible tumor agnostic approach to test the efficacy of CPB in pts at high risk for recurrence. Future studies will assess the impact of CPB in MRD-positive MMRd tumors.

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