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Abstract CT003: Non operative management of mismatch repair deficient tumors FREE

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Abstract

Background:

Neoadjuvant checkpoint blockade of locally advanced mismatch repair deficient (MMRd) rectal cancers results in a high rate of complete clinical responses that can eliminate the need for surgery. MMRd occurs broadly across solid tumors but is unknown if these findings could be extended in a tumor agnostic manner.

Methods:

Early stage MMRd solid tumors that were eligible for curative intent surgery were enrolled to a study of six months of neoadjuvant treatment with dostarlimab, a PD-1 blocking monoclonal antibody. The study was comprised of two cohorts. The first cohort enrolled MMRd locally advanced rectal cancers and the second cohort enrolled MMRd non rectal solid tumors. In both cohorts, patients who achieved a clinical complete response could elect non-operative management. The co-primary endpoints for cohort one included response rate and durability of complete response at 12 months, the primary endpoint for cohort two was response and exploratory endpoints included genomic and circulating tumor DNA analyses for both cohorts.

Results:

110 patients were enrolled. In cohort one (MMRd rectal cancers), to date, 48 patients completed 6 months of treatment and 100% achieved a clinical complete response and did not undergo surgical resection of their primary tumor. Twenty nine of these 48 have attained 12 or more months of recurrence-free survival median 24.8 (range 15.6,48.6). In the second cohort of locally

advanced MMRd non-rectal solid tumors, which included esophagogastric, hepatobiliary, genitourinary, and gynecologic tumors, at time data submission, 49 patients completed treatment and 31 patients (63%) achieved a clinical complete response and did not undergo resection surgical resection of their primary tumor. Across both cohorts, 81% of patients (79 of 97) who completed 6-months of treatment achieved a clinical complete response and 79% (77 of 97) were managed non-operatively. Baseline tumor mutational burden and MSI sensor scores in cohort one was 55.2 mutations per megabase (range 22.8, 106) and 19 (range 2.2, 37.6),and for cohort two 51.1 mutations per megabase (range 4.9, 145) and 18.6 (range 0.23, 39.4), respectively. Tumor-informed circulating tumor DNA levels were detectable at baseline in 87% of patients and on-therapy levels correlated with complete and incomplete responses especially at the completion of treatment.

Conclusion:

In the curative setting, neoadjuvant PD-1 blockade offers the option of organ preservation for most patients with early stage MMRd malignancies regardless of tumor type.

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