LBA5 **Oral Abstract Session**

Single agent PD-1 blockade as curative-intent treatment in mismatch repair deficient locally advanced rectal cancer.

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Background: Neoadjuvant chemotherapy and radiation followed by surgical resection of the rectum is a standard treatment for locally advanced rectal cancer. A subset of rectal cancer is mismatch repair deficient. Since mismatch repair deficient colorectal cancer is responsive to PD-1 blockade in the metastatic setting, we hypothesized that locally advanced mismatch repair deficient rectal cancer is sensitive to checkpoint blockade and may alter the requirements for chemoradiotherapy and surgery. **Methods:** We conducted a prospective phase II study in which single agent dostarlimab, an anti PD-1 monoclonal antibody, was administered every 3 weeks for 6 months in patients with mismatch repair deficient stage II and III rectal adenocarcinoma, to be followed by standard chemoradiation and surgery. Patients who achieved a clinical complete response were eligible for omission of chemoradiation and surgery. **Results:** Twelve patients initiated treatment and have at least 6 months of follow up. All 12 (100%, 95% CI:74%-100%) achieved a clinical complete response with no evidence of tumor on MRI, FDG-PET, endoscopic visualization, digital rectal exam, or biopsy, which satisfied the study's co-primary endpoint. To date, no patients have required chemoradiation or surgery, and no cases of progression or recurrence have been noted during follow up (range 6-25 months). No serious adverse events > grade 3 were observed. **Conclusions:** Mismatch repair deficient locally advanced rectal cancer is exceptionally sensitive to single agent PD-1 blockade. Longer follow up is needed to assess response duration. Clinical trial information: NCT04165772. Research Sponsor: Stand Up to Cancer, Swim Across America, Simon and Eve Colin Foundation, Pharmaceutical/Biotech Company, U.S. National Institutes of Health.