Background For patients with microsatellite stable or mismatch repair proficient (MSS/pMMR) metastatic colorectal cancer, immune checkpoint blockade does not work. Strategies are being devised where immunotherapy is being combined with other novel agents or radiopharmacology to enhance PD-L1 expression, alter the tumor microenvironment (turning ‘cold’ tumors ‘hot’) and/or release neoantigens to enhance efficacy of immune checkpoint blockade. We chose Yttrium-90 radioembolization (Y90-RE) in combination with a fixed dose of of immunotherapy given pre- and post-Y90-RE as a treatment strategy to be examined as part of a clinical trial for those patients with metastatic colorectal cancer who have liver-predominant or liver-only metastases.

Methods This clinical trial will be conducted as a single-center, open-label, Phase I/2 trial to evaluate the feasibility and safety of Yttrium-90 radioembolization (Y90-RE) in combination with a fixed dose of of immunotherapy (durvalumab - 750 mg) in subjects with liver-predominant, metastatic colorectal cancer (mCRC), which is mismatch repair proficient/microsatellite stable (pMMR/MSS). As noted on clinicaltrials.gov, the purpose of this clinical trial is to find out more about the side effects of immunotherapy with a form of radiation treatment for the cancer in the liver called Yttrium-90 RadioEmbolization (Y90-RE). An immunotherapy drug, durvalumab, will be given intravenously every 2 weeks. We are studying what doses of durvalumab are safe for people in combination with this form of radiation treatment. Patients in this study will receive durvalumab, which is experimental and not approved by the U.S. Food and Drug Administration (FDA) for metastatic colorectal cancer. Microscopic radioactive particles (TheraSphere®) will be used for radioembolization to deliver the Y90 drug to the liver. The number of doses of the immunotherapy drug (range: 2 to 5) will depend on the cohort patients are assigned to. There is no placebo. Everyone on the study is treated with immunotherapy alongside the Y90-RadioEmbolization (table 1). Primary objective is to look at safety and feasibility of this approach.

Once the recommended phase-2 dose is determined through an acceleration titration design, a total of 18 patients are being planned to be treated on this study at the University of Iowa Holden Comprehensive Cancer Center. The study has strong correlational components from a tumor microenvironment (pre- and post-biopsies) as well as ‘liquid biopsies’ - circulating tumor DNA (ctDNA) testing already integrated into the protocol. This would provide an opportunity to understand better the changes to the tumor microenvironment from such an approach in addition to understanding mechanisms of immune evasion/resistance.

Conclusions N/A

Trial Registration NCT04108481

REFERENCES

Abstract 331 Table 1 Dose escalation cohort of durvalumab.

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Abstract 332 NOVEL TGF-β SIGNATURES IN METASTATIC COLORECTAL CANCER PATIENTS TREATED WITH VACTOSERTIB IN COMBINATION WITH PEBVOLIZUMAB


REFERENCE


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