Clinical Trial Completed

A SAFETY AND FEASIBILITY STUDY OF THE ORAL LIVE BIOThERAPEUTIC MRx0518 WITH HYPOFRACTIONATED PREOPERATIVE RADIATION FOR RESECTABLE PANCREATIC CANCER

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Background Pancreatic ductal adenocarcinoma (PDAC) is the third leading cause of cancer-related deaths in the United States necessitating novel therapeutic strategies. Surgical resection of PDAC remains the only curative option for patients, with microscopic R0 resection being a requisite for curative therapy. In this respect, neoadjuvant therapy is increasingly being administered to patients with resectable PDAC in an attempt to maximize the likelihood for long-term survival. Simultaneously, the role of the intestinal microbiota in systemic immune responses has gained attention. Manipulating the gut microbiome, particularly through the administration of MRx0518, a strain of commensal Enterococcus gallinarum, has demonstrated encouraging results in preclinical models, stimulating immune responses and displaying anti-tumor activity. We thus hypothesize that augmenting the microbiota with MRx0518 can elicit an immunogenic profile that may be beneficial in decreasing systemic failure and improving local control in the setting of resectable pancreatic cancer. In this study, we aim to evaluate the safety and tolerability of MRx0518 in combination with hypofractionated neoadjuvant chemoradiation in PDAC.

Methods Safety and tolerability of MRx0518 in combination with preoperative hypofractionated radiation was assessed in eligible patients diagnosed with resectable PDAC. Patients were administered MRx0518 twice daily starting one week prior to initiating chemoradiation with 30Gy in 10 fractions. Patients continued to receive MRx0518 up to 24 hours prior to surgery for tumor resection if deemed eligible. The primary endpoint of the study was safety as assessed by the occurrence of Grade 3 toxicities defined by CTCAE v5.0 up to 30 days after completion of treatment with MRx0518 in combination with chemoradiation.

Results A total of 15 patients were screened with resectable pancreatic ductal adenocarcinoma, and 13 eligible patients were analyzed in the study. Treatment related adverse events of any grade were reported in 4 patients (30.8%); these included fatigue, nausea, diarrhea, and abdominal pain. No patients experienced Grade 3 toxicities. At a median follow-up of 14.6 months amongst all patients, median overall survival had not been reached. A total of 7/13 patients underwent surgical resection, with a median recurrence free survival of 19.2 months. All resected patients exhibited negative margins. No major pathologic response was observed in patients who underwent resection.

Conclusions The administration of MRx0518 with hypofractionated neoadjuvant chemoradiation in resectable PDAC was well tolerated. Further analysis of immune cell infiltrates within resected tumors will help reveal further associations to changes in the local microbiome.

Trial Registration NCT04193904

Ethics Approval The trial protocol was approved by the Institutional Review Board of MD Anderson Cancer Center under protocol #2019-0540. The trial was done in accordance with the International Conference on Harmonisation Guidelines on Good Clinical Practice and the Declaration of Helsinki. All patients gave informed consent before taking part in the study.

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