ATEZOLIZUMAB AND BEVACIZUMAB PRE-LIVER TRANSPLANTATION FOR PATIENTS WITH HEPATOCELLULAR CARCINOMA BEYOND MILAN CRITERIA: TRIAL IN PROGRESS

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Background Hepatocellular carcinoma (HCC) represents the second most common cause of cancer-related death and accounts for over 80% of primary liver cancers worldwide. However, in 90% of patients, HCC occurs in the setting of cirrhosis where optimal management remains liver transplantation (LT) with 5-year survival rates of approximately 80%. Therapeutic blockade of PD-L1 binding by atezolizumab has been shown to enhance the magnitude and quality of tumor-specific T cell responses, resulting in improved anti-tumor activity. Bevacizumab is a recombinant humanized monoclonal IgG1 antibody that binds to and inhibits the biologic activity of human vascular endothelial growth factor (VEGF) in vitro and in vivo assay systems. We hypothesize that atezolizumab and bevacizumab can appropriately bridge patients with HCC beyond MC to transplantation and not increase the risk of 1-year post-transplant rejection. To test this hypothesis, patients with HCC beyond Milan Criteria (in brief, 5 – 10 cm), who are transplant-eligible will be treated with 6 months of neoadjuvant/downstaging atezolizumab plus bevacizumab while receiving standard of care transarterial chemoembolization (TACE). The proposed clinical trial will evaluate the feasibility of using a combination of the chemotherapeutic interventions atezolizumab and bevacizumab in a group of patients with HCC who have tumors beyond the Milan Criteria in order to bridge them to liver transplantation.

Methods This is a Phase II multi-site study, a site in the US and a site in Canada. Combined enrollment from these sites will be up to 30 patients. Atezolizumab will be administered as a 1200mg intravenous infusion followed by bevacizumab 15mg/kg on the same day. The regimen will be administered every three weeks for up to 8 cycles (or 6 months) in pre-Liver Transplantation patients with HCC. The primary objective of this study is to assess the feasibility and safety of transplantation post atezolizumab/bevacizumab for patients with HCC beyond Milan criteria. The secondary endpoints include ORR of participants who enroll in the study, DFS at 1-year in participants who undergo a liver transplant, defined as time to disease recurrence or death, whichever is earlier, from time of liver transplant, and OS in patients from the time of study enrollment to death from any cause as well as from the time of transplant to death from any cause. An interim analysis will be performed to assess the feasibility and safety after 20 patients become evaluable. The study is open with 30 patients enrolled at the time of submission. Clinical trial information: NCT05185505.