ABATACEPT FOR IMMUNE CHECKPOINT INHIBITOR ASSOCIATED MYOCARDITIS (ATRIUM): A PHASE 3, INVESTIGATOR-INITIATED, RANDOMIZED, DOUBLE BLIND, PLACEBO-CONTROLLED TRIAL

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Background Patients with myocarditis secondary to treatment with an immune checkpoint inhibitor (ICI) represent a poor prognosis population with a high unmet clinical need. Data from multiple independent international cohorts have shown that the rate of major adverse cardiac events (MACE) with ICI myocarditis despite administration of corticosteroids ranges from 25-50%. Abatacept is a selective co-stimulation modulator that inhibits T cell activation by binding to CD80 and CD86, thereby blocking its interaction with CD28. In case reports, abatacept has been used to treated ICI myocarditis. The use of abatacept in ICI myocarditis is supported by animal models of ICI myocarditis, with the administration of abatacept leading to a reduction in cardiac immune activation and increased survival.

Methods The abatacept for immune checkpoint inhibitor associated myocarditis (ATRIUM) trial is designed as a phase 3, investigator-initiated, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of abatacept compared to placebo in 390 hospitalized participants with ICI associated myocarditis. Hospitalized participants diagnosed with ICI-related myocarditis, aged ≥18 years, with serum evidence of ongoing myocardial injury (troponin ≥5 times the upper limit normal), and treated, or with intent to treat, with 1000 mg of solumedrol/day are eligible. Participants will receive either abatacept (10 mg/kg) or placebo given IV followed by study drug infusion/placebo again at 24 hours and on day 14 with an optional 4th dose on day 28. The primary aim is to test whether abatacept, as compared to placebo, is associated with a reduction in MACE among participants hospitalized with myocarditis secondary to an ICI. The primary outcome, MACE, is a composite of cardiovascular death, non-fatal sudden cardiac arrest, cardiogenic shock, significant ventricular arrhythmias, significant bradyarrhythmias, or incident heart failure. Each component of the primary composite end point will be evaluated individually as a secondary endpoint, as are troponin levels, rates of deep venous thrombosis and pulmonary embolism, and incidence rates of treatment-related adverse events. Exploratory outcomes focus on cancer outcomes, healthcare utilization, quality of life, and correlative studies.

This study is recruiting at time of submission. Clinical trial information: NCT05335928.

Trial Registration NCT05335928

Ethics Approval The clinical trial protocol has been approved by the Mass General Brigham Institutional Review Board (Protocol #:2021P003690) and all participants will provide informed consent before taking part.