Clazakizumab for the Treatment of Chronic Active Antibody Mediated Rejection in Kidney Transplant Recipients

Status: Recruiting

Eligibility Criteria

Age: 18 years to 75 years old

This study is NOT accepting healthy

Healthy Volunteers: volunteers

• Inclusion criteria: 1. Age 18-75 years. 2. Living donor/deceased donor kidney transplant recipients ≥6 months from time of transplant. 3. Diagnosis of CABMR determined by kidney biopsy and the presence of HLA DSA using single-antigen bead-based assays. NOTE: If conducted within 12 months (+3 weeks) prior to the start of the screening period, and no intervening treatments have been administered, the biopsy does not need to be repeated at Screening. If conducted within 6 months (+ 3 weeks) prior to the start of Screening, the DSA analysis does not need to be repeated at screening. To be considered for determination of study eligibility, the biopsy and DSA analysis must be performed at least 2 months ± 2 weeks after the end of any prior treatment for ABMR (including CABMR) or TCMR, in order to show continuing CABMR and presence of HLA DSA. In addition, with the exception of steroids, treatments for ABMR or TCMR are not allowed within 3 months prior to the start of screening. The following histopathologic and serologic diagnostic criteria (based on Banff 2015 criteria [Loupy et al, 2017]) must be met for inclusion:

• Morphologic evidence of chronic tissue injury, as demonstrated by TG (cg>0). Biopsies without evidence of chronic tissue injury on light microscopy, but with glomerular basement membrane double contours on electron microscopy (cg1a) are eligible.

• Evidence of current/recent antibody interaction with vascular endothelium, including 1 or more of the following.

• Linear C4d staining in peritubular capillaries or medullary vasa recta (C4d2 or C4d3 by immunofluorescence on frozen sections, or C4d > 0 by immunohistochemistry on paraffin sections).

• At least moderate microvascular inflammation ([g + ptc] ≥ 2) in the absence of recurrent or de novo glomerulonephritis, although in the presence of acute TCMR, borderline infiltrate, or infection, ptc ≥ 2 alone is not sufficient and g must be ≥ 1. NOTE: The local pathologist's diagnosis must be reviewed by a central pathologist to confirm eligibility for entry into the study. Biopsies with other histopathologic changes (eg, BKV nephropathy or recurrent glomerulonephritis) may be eligible if concurrent CABMR changes (as detailed above) are present and determined to be the predominant cause of renal dysfunction. 4. Serologic evidence of circulating DSA to HLA. NOTE: The local laboratory DSA results must be reviewed and confirmed by the central HLA reviewer during the screening period.

• Exclusion criteria: 1. Multi-organ transplant recipient (except for simultaneous kidney-pancreas or previous multiple kidney transplants) or cell transplant (islet, bone marrow, stem cell) recipient. 2. Treatment for ABMR (including CABMR) or TCMR within 3 months prior to the start of screening with the exception of steroids. 3. Received T cell depleting agents (e.g., alemtuzumab, anti-thymocyte globulin) within 3 months prior to the start of screening. 4. Pregnant, breastfeeding, or unwillingness to practice adequate contraception. 5. Active tuberculosis (TB) or history of active TB. 6. History of human immunodeficiency virus (HIV) infection or positive for HIV. 7. Seropositive for hepatitis B surface antigen (HBsAg) 8. Hepatitis C virus (HCV) RNA positive.

Conditions & Interventions

Interventions:
Biological: Clazakizumab, Drug: Physiologic saline solution
Conditions:
Antibody-mediated Rejection
Keywords:
Chronic Active, Antibody-mediated Rejection (AMR)

More Information

Contact(s): Trial Registration Coordinator - clinicaltrials@cslbehring.com
Principal Investigator: Gupta, Gaurav
Phase: Phase 3
IRB
Number: HM20015883
System ID: NCT03744910