Phase 2b Study to Investigate the Safety and Efficacy of TIN816 in Sepsis-associated Acute Kidney Injury (SA-AKI)

Last Update: Mar 17, 2025

A Multicenter, Randomized, Double-blind, Placebo-controlled, Four-arm, Parallel-group, Dose-finding Phase 2b Study to Investigate the Safety and Efficacy of TIN816 Via a Single Intravenous Infusion in the Treatment of Participants With Sepsis-associated Acute Kidney Injury (SA-AKI)

ClinicalTrials.gov Identifier:

NCT05996835

Novartis Reference Number:CTIN816B12202

See if you Pre-qualify

All compounds are either investigational or being studied for (a) new use(s). Efficacy and safety have not been established. There is no guarantee that they will become commercially available for the use(s) under investigation.

Study Description

The purpose of this Ph2b study is to characterize the dose-response relationship and to evaluate the safety and efficacy of three different single doses of TIN816 in hospitalized adult participants in an intensive care setting with a diagnosis of sepsis-associated acute kidney injury (SA-AKI). This is a multicenter, randomized, double-blind, placebo-controlled, four-arm, parallel-group, dose-finding phase 2b study. The study will enroll hospitalized adult participants with a diagnosis of sepsis and acute kidney injury (AKI). The study consists of a screening period (24-48 hours), a treatment period (Day 1), and post-treatment period (Day 2 to 90). Screening will take place during hospitalization in ICU (or intermediate care unit/HDU) where potential participants will undergo screening to assess the presence of sepsis and AKI. At Treatment Day 1, participants who meet eligibility criteria at screening and baseline will be randomized in a 3:1:1:3 ratio to receive a one-time treatment of TIN816 or placebo by intravenous infusion in a participant and investigator-blinded fashion. Treatment Day 1 is followed by a 90-day post-treatment period for safety and efficacy assessments. An interim analysis (IA) is planned when approximately 120 participants complete Day 30 visit. A final analysis will be performed after all participants have completed Day 90.

Condition

Acute Kidney Injury Due to Sepsis

Phase

Phase2

Overall Status

Recruiting

Number of Participants

320

Start Date

Jan 18, 2024

Completion Date

Feb 20, 2026
Gender
All
Age(s)
18 Years - 85 Years (Adult, Older Adult)

Interventions

Other

Placebo

0.9% sterile saline solution
Biological

TIN816 70 mg lyophilisate powder

Immunotherapy Recombinant human CD39 enzyme

Eligibility Criteria

Inclusion Criteria:

1. Signed informed consent must be obtained prior to participation in the study.
2. ≥ 18 to ≤ 85 years of age
3. Admitted to ICU or intermediate care unit/ high dependency care unit (HDU)
4. Diagnosis of sepsis according to criteria defined by The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) based on:

* Suspected or confirmed infection AND
* Acute increase of SOFA score of 2 or more (excluding renal component). The baseline SOFA score should be assumed to be zero unless the participant is known to have pre-existing (acute or chronic) organ dysfunction before the onset of infection
5. Diagnosis of AKI Stage 1 or greater per the following criterion at randomization:

An absolute increase in serum or plasma creatinine by ≥ 0.3 mg/dL (≥ 26.5 µmol/L) within 48 hours or presumed to have occurred in the previous 48 hours as compared to the reference serum creatinine.

* For participants with hospital-acquired AKI, a stable serum creatinine obtained in the hospital prior to AKI diagnosis should be used as the reference serum creatinine.
* For participants presenting from community, the reference serum creatinine should be estimated using the following order of preference:

1. The most recent value within 3 months of the hospital admission. If not available:
2. The most recent value between 3 and 12 months prior to hospital admission. If not available:
3. At hospital admission

Exclusion criteria

1. Not expected to survive for 24 hours
2. Not expected to survive for 30 days due to medical conditions other than SA-AKI

3. History of CKD with a documented estimated GFR \<45 mL/min prior to admission to hospital
4. eGFR \<45mL/min at admission without any other reference serum eGFR within last 12-months
5. Receiving RRT or a decision has been made to initiate RRT within 24 hours after randomization
6. Weight is less than 40 kg or more than 125 kg.
7. Limitations to the use of mechanical ventilation, RRT or vasopressors/inotropes (N.B. limitations on Cardiopulmonary resuscitation (CPR)e.g., do-not-resuscitate orders are not an exclusion criterion unless associated with likely poor outcome in next 24 hours)
8. Sepsis diagnosis according to sepsis inclusion criteria for a period longer than 72 hours prior to ICU admission
9. AKI diagnosis according to AKI inclusion criteria over 48 hours after admission to ICU
10. Inability to administer study drug within 24 hours of diagnosis of AKI according to AKI inclusion criteria
11. Presence of AKI, in the Investigator's opinion, as suggested by clinical manifestation, e.g., prolonged oliguria or severe renal dysfunction on admission without a history of CKD, for a period longer than 24 hours prior to study drug administration
12. Evidence of recovery from AKI based on the investigator's clinical judgement prior to randomization
13. AKI is most likely attributable to other causes than sepsis, such as nephrotoxic drugs (Non-steroidal anti-inflammatory drugs (NSAIDs), contrast, aminoglycosides, etc.) or renal perfusion-related (acute abdominal aortic aneurysm, dissection, renal artery stenosis), urinary obstruction
14. Documented (biopsy proven) or suspected history of acute or sub-acute kidney diseases such as rapidly progressive glomerular nephritis (RPGN) and acute interstitial nephritis (AIN)
15. Patients who are post-nephrectomy
16. Patients with permanent incapacitation
17. Patients who are thrombocytopenic at screening (platelet count \<50,000 per microliter) who have active/uncontrolled bleeding or who present current or past conditions indicating high risk for bleeding in the opinion of the investigator (e.g. coagulopathies, previous history of major non-traumatic bleeding etc.)
18. Immunosuppressed patients

* History of immunodeficiency diseases
* Receiving immunosuppressant treatment or on chronic high doses (high-dose therapy exceeding 2 weeks of treatment) of steroids equivalent to prednisone/prednisolone 0.5 mg/kg/day, including solid organ transplant patients. Patients with septic shock treated with corticosteroids (as per the Surviving Sepsis Guidelines) can be included. See Appendix Section 10.6 Immunosuppresant drugs, (Table 10 5 Immunosuppressant drug exclusions)
19. Patients with known or presumed latent or active TB based on clinical history or imaging e.g. patients on TB preventive therapy or close/household contacts of pulmonary TB patients
20. Known active hepatitis B or C infection, or positive Hepatitis B Virus (HBV) or Hepatitis C Virus (HCV) serology or patients with advanced chronic liver disease, confirmed by a Child-Pugh score of 10-15 (Class C)
21. Acute pancreatitis with no established source of infection
22. Active hematological malignancy (previous hematological malignancies that are not actively treated are allowable)
23. Burns requiring ICU treatment
24. Sepsis attributed to confirmed COVID-19
25. Use of other investigational drugs within 5 half-lives of enrollment, within 30 days (e.g., small molecules) or until the expected pharmacodynamic effect has returned to baseline (e.g., biologics), whichever is longer; or longer if required by local regulations
26. History of hypersensitivity to the study treatment or its excipients or to drugs of similar chemical classes
27. Any medical conditions that could significantly increase risk of participants' safety by participating in this study according to investigator's judgement

28. Women with a positive pregnancy test, pregnancy or breast feeding
29. Women of childbearing potential, unless they are using highly effective methods of contraception for the entire duration of the trial.

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