RESTORE

TRAVERE™ THERAPEUTICS

RESTORE STUDY (Cheno-CTX-301) OVERVIEW — ADULT GROUP

STUDY INTRODUCTION

Travere Therapeutics, a biopharmaceutical company that specializes in developing drugs for rare diseases, is sponsoring a global clinical study, called RESTORE, in adults, teenagers, and children who have been diagnosed with cerebrotendinous xanthomatosis (CTX). The purpose of the study is to evaluate the safety and efficacy (how well the study drug works) of chenodeoxycholic acid (an investigational bile acid replacement therapy also called Chenodal™, or CDCA) in people with CTX.

CTX is a rare, progressive, and underdiagnosed bile acid synthesis disorder affecting many parts of the body. Patients with CTX have a genetic mutation that prevents their body from making CDCA. As a result, the body is unable to break down cholesterol properly, causing toxins (e.g., cholestanol and bile alcohols) to build up throughout the body over time. In CTX, cholestanol builds up in the eyes, tendons (tissues that connect muscle to the bone), brain, and other tissues and can cause a number of different problems throughout a patient's life.

The investigational medicine in the RESTORE study, CDCA, is a bile acid replacement therapy that is recognized as a potential treatment for CTX[1,2]; however, it has not been approved by the U.S. Food and Drug Administration (FDA) for use in CTX in the United States. CDCA is approved in the United States as Chenodal™ for the treatment of a certain type of gallstones.[3]

The goal of the RESTORE study is to better understand how the body responds, as measured in blood and urine, when people with CTX use CDCA. It will also help the sponsor (Travere Therapeutics, Inc.) learn more about the safety of CDCA, or what side effects, if any, appear with CDCA use. For the purposes of the RESTORE study, CDCA is considered to be an investigational study drug.

STUDY OVERVIEW

The study has 2 groups: Pediatric and Adult. The Adult Group will include patients who are 16 years old and older. The study lasts about 25 to 28 weeks (6-7 months). During this time, all patients will need to make approximately 18 trips to the study center to complete visits with the study doctor. The goal is to include about 12 patients in the Adult Group. For information on the Pediatric Group of the RESTORE study (1 month to 15 years of age), please see CTXRestore.com or the Pediatric study flyer.

KEY ADULT ELIGIBILITY CRITERIA

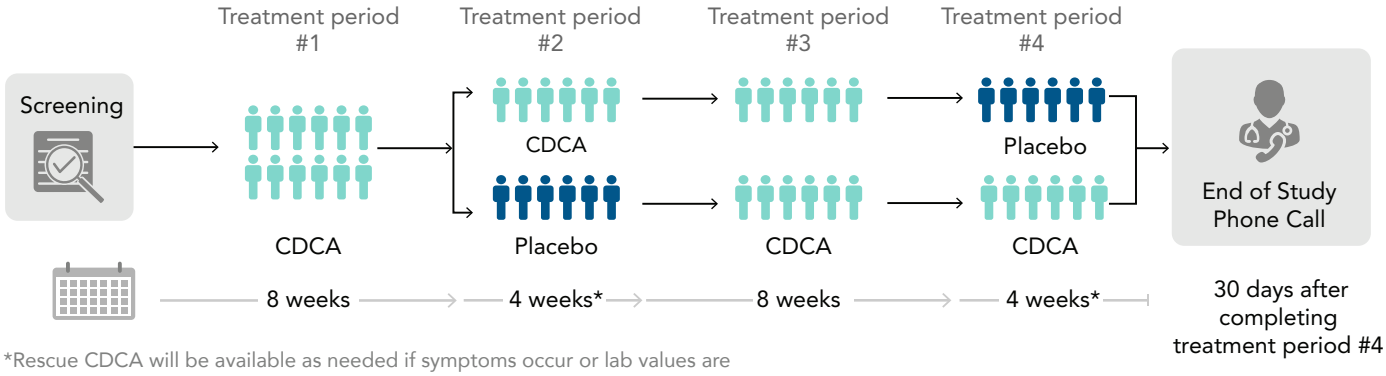
1. Male or female, at least 16 years of age at the time of screening
2. Clinical diagnosis of CTX (presence of symptoms) with supporting laboratory results (for example, increased cholestanol and bile alcohols in blood or urine)
3. Male and female participants of childbearing potential must agree to use reliable birth control throughout the study

You must meet all other study criteria to take part in the RESTORE study. The full list of eligibility criteria is available at clinicaltrials.gov/ct2/show/NCT04270682

For more information, visit clinicaltrials.gov/ct2/show/NCT04270682 or CTXRestore.com or contact medinfo@travere.com

ADULT GROUP

For adults, this study involves a **Screening period** (4 weeks), four **Treatment periods** (totaling 6 months), and a **Follow-up Phone Call**.



*Rescue CDCA will be available as needed if symptoms occur or lab values are out of the expected range for patients receiving CDCA or placebo.

Study drug will be given in a tablet form to adult patients.

At **Screening**, a physical exam will be performed, and blood and urine will be collected to determine if this study is right for you or your child. If your doctor thinks you are eligible to participate in the study and you agree, you may then begin the **Treatment period**. As shown in the Figure, the Treatment period consists of 4 phases:

1. **Treatment period #1:** All patients will take CDCA by mouth 3 times daily for 8 weeks. Visits with the study doctor will occur every 2 weeks for a health check and blood/urine collection.
2. **Treatment period #2:** Patients will be randomly assigned either to continue CDCA as before, or take placebo tablets 3 times daily for the next 4 weeks. Visits with the study doctor will occur every week for a health check and blood/urine collection.
3. **Treatment period #3:** All patients will take CDCA by mouth 3 times daily for 8 weeks. Visits with the study doctor will occur every 2 weeks for a health check and blood/urine collection.
4. **Treatment period #4:** Patients will take the alternative treatment that they did not take in Treatment period #2. This means that patients who took placebo in Treatment period #2 will now take CDCA and patients who took CDCA in Treatment period #2 will now take placebo. Visits with the study doctor will occur every week for a health check and blood/urine collection.

If the change in urine bile alcohols in your urine exceed a pre-set limit or you experience worsening of symptoms related to CTX, you may be switched to rescue CDCA.

Follow-up Phone Call: Approximately 30 days after the last dose of study drug, patients will receive a phone call from the study center to check up on them.

WHAT MUST PATIENTS DO FOR THIS STUDY?

1. Patients must attend study doctor visits and participate in the required assessments, which may vary by visit, and include:
   a. Interviewing you and assessing your overall health
   b. Monitoring vital signs (such as blood pressure)
   c. Evaluating heart (by electrocardiogram, or ECG), brain function (by electroencephalogram, or EEG), and eyes (ophthalmology exam)
   d. Collecting blood and urine samples
2. Patients must collect urine samples at home prior to a study visit, refrigerate the samples while at home, and then transport the urine samples to the study center for each visit
3. Patients must take study drug as directed and follow directions provided by study staff
4. Patients must complete health questionnaires at home and during doctor visits
5. Patients must complete a paper and electronic diary to record information about the study drug, at-home urine collections, changes in symptoms, and quality of life
6. Patients must use appropriate birth control methods throughout participation in the study

REFERENCES: 1. Mignarri A, Gallus GN, Dotti MT, Federico A. A suspicion index for early diagnosis and treatment of cerebrotendinous xanthomatosis. *J Inherit Metab Dis*. 2014;37(3):421-429. 2. National Organization for Rare Disorders. Rare Disease Database: Cerebrotendinous xanthomatosis. https://rarediseases.org/rare-diseases/cerebrotendinous-xanthomatosis/ Accessed April 26, 2020. 3. CHENODAL [package insert]. Fort Collins, CO: Manchester Pharmaceuticals, Inc; 2009.