CHAGAS DISEASE

Searching for shorter, safer, more effective treatments to stop a silent killer

Chagas disease, also known as American trypanosomiasis, is a life-threatening disease caused by the *T. cruzi* parasite, which is spread mainly by the bite of the 'kissing bug'. In Latin America, it causes more deaths than any other parasitic disease. Although Chagas can go unnoticed for years, it can eventually cause irreversible damage to the heart and other vital organs. An estimated 70 million people are at risk, and only 10% of people living with the infection are diagnosed. Current treatments for the disease were discovered over 50 years ago, must be taken for at least eight weeks, and sometimes have serious side effects. Human migration is expanding the distribution of Chagas, mainly in the Americas and Europe, and vector-borne transmission is increasing in new geographies due to climate change and deforestation.

The push for progress

Together with our partners, DNDi delivered the first formulation of the drug benznidazole for infants and children with Chagas in 2011 and later piloted a simplified model of care for adults and children, promoting 'test-and-treat' approaches in Colombia, Guatemala, and Argentina. In 2009, we established the Chagas Clinical Research Platform, now a network of over 500 members from more than 120 institutions in 24 countries working to address research gaps, coordinate the response, promote scientific exchange, and advocate for access to diagnosis and treatment with and for people most at risk.

Our goal is now **to improve current treatments in the near term by developing a safer, shorter treatment with benznidazole. We aim to help limit mother-to-child transmission through targeted treatment of women of childbearing potential and help strengthen access to prompt diagnosis and treatment of newborns, for whom early treatment with existing medicines is highly efficacious.** Our teams are also working to reach more people living with Chagas disease in remote areas in Latin America by simplifying diagnosis, treatment, and tests of cure. Looking to the longer term, we are working to discover and develop entirely new medicines – with the aim of launching at least one Phase III trial by 2028.

Delivering safer, shorter treatments

Alongside our focus on accelerating access to testing and treatment with partners in Latin America, our teams have continued work to develop improved treatment regimens based on existing drugs for Chagas. Together with partners including the Fundación Mundo Sano and Laboratorio Elea Phoenix, DNDi reinitiated the NuestroBen clinical trial in Argentina, with the first participant in the redesigned trial enrolled in August 2023.

The objective of NuestroBen is to compare the safety and efficacy of shorter benznidazole regimens for the treatment of chronic Chagas disease of indeterminate form or with mild cardiac progression – with shorter treatment durations potentially

FACTS

>6 million
people living with Chagas worldwide

About 35%
experience cardiac or other organ damage

The disease is endemic in 21 countries in the Americas

DNDi
Best Science for the Most Neglected

Photo credit: Ana Ferreira-DNDi

> **“The doctor explained that Chagas disease affects the organs and the heart. Because I was pregnant, she couldn’t treat me at that time – only after the child was no longer being breastfed. I kept thinking, I hope my baby isn’t born with this.**

Sara lives in Colombia with her husband and three children. She remembers playing with kissing bugs in bottles when she was little. When she was diagnosed, she realized that she must have had Chagas for a long time.

maintaining efficacy while minimizing side effects and encouraging adherence. The redesigned study protocol allows results to be compared across NuestroBen and Benlatino, a similar trial led by the Oswaldo Cruz Foundation that will take place in Colombia and Bolivia. By the end of 2023, four study sites were opened in Buenos Aires and northern Argentina, with a total of 300 participants expected to be recruited by the first quarter of 2025. The Chagas Clinical Research Platform played an active role in the design of both trials, ensuring that results can be harmonized to deliver robust scientific evidence for safer, shorter benznidazole treatment regimens in Latin America.

Advancing towards a test of cure and disease progression

A major challenge for test-and-treat strategies – and the development of new treatments for Chagas disease – is the lack of analytical tools suitable for monitoring disease progression and response to treatment at the point of care. Working with InfYnity Biomarkers, we are now at an advanced stage of developing and testing the MultiCruzi assay as a simple test of cure with potential for use in decentralized healthcare settings. In 2023, analysis of samples from two clinical trials using MultiCruzi showed promising results, allowing for adequate measurement of reductions in serum antibody levels – an indicator of parasitological cure.

Tackling the urgent need for innovation

New drugs that can cure Chagas disease and prevent the development of life-threatening complications are urgently needed. In 2023, DNDi and partners advanced drug discovery projects aimed at identifying and developing all-new treatments suitable for children and women of childbearing potential.

Working with the University of Washington (UW), University of Dundee Drug Discovery Unit, and GSK, DNDi continued to optimize a new generation of *T. cruzi* inhibitors in the UW series of compounds. First identified at the UW, the novel mode of action and promising efficacy profile of leads from the series suggest the possibility of providing a single-compound cure for Chagas disease.

Earning recognition as DNDi’s 2023 Project of the Year in pre-clinical research, collaborations to identify new hit series from new collections of compounds from both natural and synthetic origins advanced with support from partners including Institut Pasteur Korea, Nagasaki University, Swiss Tropical and Public Health Institute, and University of Dundee. In parallel, several promising compounds identified in previous years entered hit-to-lead projects in 2023, and ongoing hit-to-lead projects continued to progress with support from partners including Mitsubishi Tanabe Pharma Corporation, with at least two chemical series with advanced leads showing promising efficacy in translational models.