

- PRESS RELEASE -

Study shows dramatically shorter treatment for Chagas disease could be just as effective, and significantly safer

Results could help remove one of the barriers to treatment scale up and bring new hope for people with Chagas disease

Barcelona/Río de Janeiro, 14 March 2019- A two-week treatment course for adult patients with chronic Chagas disease showed, when compared to placebo, similar efficacy and significantly fewer side effects than the standard treatment duration of eight weeks, according to the results of a clinical trial in Bolivia led by the Drugs for Neglected Diseases initiative (DNDi).

Chagas disease affects an estimated six million people globally and can lead to irreversible damage to vital organs, and death. Benznidazole, one of the two drugs used to treat Chagas, is traditionally administered twice a day over a course of eight weeks, in line with PAHO and WHO recommendations and national guidelines.

The Phase II clinical trial, carried out in three centres in Bolivia, sought to improve safety, tolerability and efficacy of treatment with this drug, which was discovered half a century ago. Initiated in 2016, it was the first-ever placebo-controlled study to test various lengths and dosages of treatment with benznidazole, both on its own as a monotherapy, and in combination with fosravuconazole.

The results were presented for the first time today at the “XV Workshop on Chagas Disease”, organised by the Barcelona Institute for Global Health (ISGlobal, a centre supported by “la Caixa”). “We believe treatment can spare people with Chagas the risk of a lifetime of debilitating complications associated with the disease. However, the current treatment can cause severe side effects, which has often discouraged some people from seeking treatment and healthcare workers from recommending it,” said Joaquim Gascon, a principal investigator in the trial and the director of the Chagas Initiative at ISGlobal.

“We’ve shown that shorter treatment could be just as effective, and much safer. This could change the paradigm for Chagas treatment, by improving adherence and encouraging wider adoption by the medical community”, said Dr Faustino Torrico, President of CEADES Foundation, Bolivia, and a principal investigator in the trial.

All arms of the study, both monotherapy and combination, were shown to be efficacious. Eighty percent of the patients assigned to the group which took the standard dose of 300mg/day of benznidazole, but for two weeks instead of the standard eight weeks, showed no sign of the parasite in their blood six and 12 months after finishing the treatment. A similar result was observed in the group that took the standard eight-week treatment.

Significantly, none of those in the two-week reduced duration group interrupted treatment. On average, 2 in 10 patients who followed the standard course of treatment with benznidazole abandoned the treatment due to side effects.

“These results bring new hope for people living with this silent disease and could change the reality of access to treatment in endemic countries. With a much simpler treatment regimen, there is no excuse for not treating people with Chagas disease,” said Dr Sergio Sosa Estani, Head of Chagas Clinical Programme at DNDi. “DNDi will now continue to work with national programmes, partners and ministries of health of endemic countries to confirm these results

and encourage necessary steps to register the new regimen and turn this breakthrough discovery into a reality for people affected by the disease.”

The trial was conducted in partnership with CEADES (Fundacion Ciencia y Estudios Aplicados para el Desarrollo en Salud y Medio Ambiente), ISGlobal, Japanese pharmaceutical company and manufacturer of fosravuconazole Eisai Co. Ltd., Argentinian pharmaceutical company manufacturer of benznidazole Elea and associated non-profit foundation Fundación Mundo Sano, among others, and funded by the Global Health Innovative Technology Fund (GHIT).

DNDi continues to work on pre-clinical and clinical research to discover, develop, and test new drugs and drug combinations to treat Chagas.

About the study

The “Bendita” study (Benznidazole New Doses Improved Treatment & Associations) was carried out in sites in Cochabamba, Tarija and Sucre, Bolivia. It tested, against a placebo, six treatment arms with a variety of lengths and dosages of benznidazole, both as a monotherapy and in combination with fosravuconazole:

- The standard 8-week treatment, with a standard daily dose of 300mg/day of benznidazole in monotherapy
- A 4-week treatment with a daily dose of 300mg/day of benznidazole in monotherapy
- A 2-week treatment with a daily dose of 300mg/day of benznidazole in monotherapy
- A 4-week treatment with a lower daily dose of 150mg/day of benznidazole in monotherapy
- A 4-week treatment with a lower daily dose of 150mg/day of benznidazole, in combination with fosravuconazole
- An 8-week treatment, with a lower weekly dose of 300mg of benznidazole, in combination with fosravuconazole.

Efficacy was measured through sustained parasitological response at six months, with a final assessment at 12 months after the end of the treatment.

For more information about the study, please read the **briefing document**.

About Chagas disease

Chagas disease, or American trypanosomiasis, is a neglected tropical disease (NTD) endemic in 21 countries in Latin America, but present also in North America, Europe, Japan, and Australia. The Pan-American Health Organisation (PAHO) estimates that the disease affects approximately 6 million people, with 30,000 new cases and 14,000 deaths per year

It is caused by the parasite *Trypanosoma cruzi* (*T. cruzi*) and transmitted by insects known as “kissing bugs”. It can also be transmitted from an infected mother to a child, or through blood transfusion or food contaminated with the vector. Since it was first discovered in 1909, Chagas has primarily affected poor, vulnerable populations with limited access to healthcare. As the disease typically remains asymptomatic for years after infection, most people with the disease are unaware of their condition. For 30-40% of people infected, the disease progresses to a late chronic stage. Of these, most will suffer cardiac damage, often leading to sudden death or progressive heart failure. The disease can also cause enlargement of the gastrointestinal tract and organs and gastrointestinal motor disorders.

There are currently only two drugs available to treat Chagas disease - nifurtimox and benznidazole - both discovered half a century ago. Treatment with benznidazole, the most

commonly used, lasts 60 days and may have undesirable side effects such as gastric intolerance, cutaneous rashes, or neuromuscular problems, amongst others. Around 20% of those who start the treatment do not complete it, mostly due to undesirable side effects.

About DNDi

A not-for-profit research and development organization, DNDi works to deliver new treatments for neglected patients, in particular those suffering with Chagas disease, sleeping sickness (human African trypanosomiasis), leishmaniasis, filarial infections, mycetoma, paediatric HIV, and hepatitis C. Since its inception in 2003, DNDi has delivered eight new treatments. DNDi's strategy for Chagas disease consists of three pillars: improving diagnostic and therapeutic tools through innovation in research & development, fostering collaboration and strengthen capacity in endemic countries through a scientific platform, and increasing patients' access to diagnosis and treatment.

About ISGlobal

The Barcelona Institute for Global Health, ISGlobal, is the fruit of an innovative alliance between "la Caixa" and academic and government institutions to contribute to the efforts undertaken by the international community to address the challenges in global health. ISGlobal is a consolidated hub of excellence in research that has grown out of work first started in the world of health care by the Hospital Clínic and the Parc de Salut MAR and in the academic sphere by the University of Barcelona and Pompeu Fabra University. The pivotal mechanism of its work model is the transfer of knowledge generated by scientific research to practice, a task undertaken by the institute's Education and Policy and Global Development departments. ISGlobal a member of the CERCA programme of the Generalitat de Catalunya

About CEADES

Fundación CEADES is a non-profit organisation working to contribute to the knowledge and the solution of health and environment problems in Bolivia, with emphasis on research and treatment of Neglected Tropical Diseases. CEADES also carries out capacity building activities for healthcare workers, community education and innovative projects about health and society and technology transfer. Since 2008, it has developed specialised healthcare models in seven centres which are part of the Platform for comprehensive care to adults with Chagas disease. In the area of scientific research, CEADES participates in various clinical trials with new medicines and biomarkers for disease cure and progression. CEADES works in collaboration with ISGlobal and with funding from AECID. In addition, it implements projects in collaboration with DNDi, Mundo Sano Foundation, UTEP, INH and HORIZON2020. At the local level, it supports institutional networks, patients' social organisations and coordinates with government agencies such as the National Chagas Programme and the Ministry of Health.

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