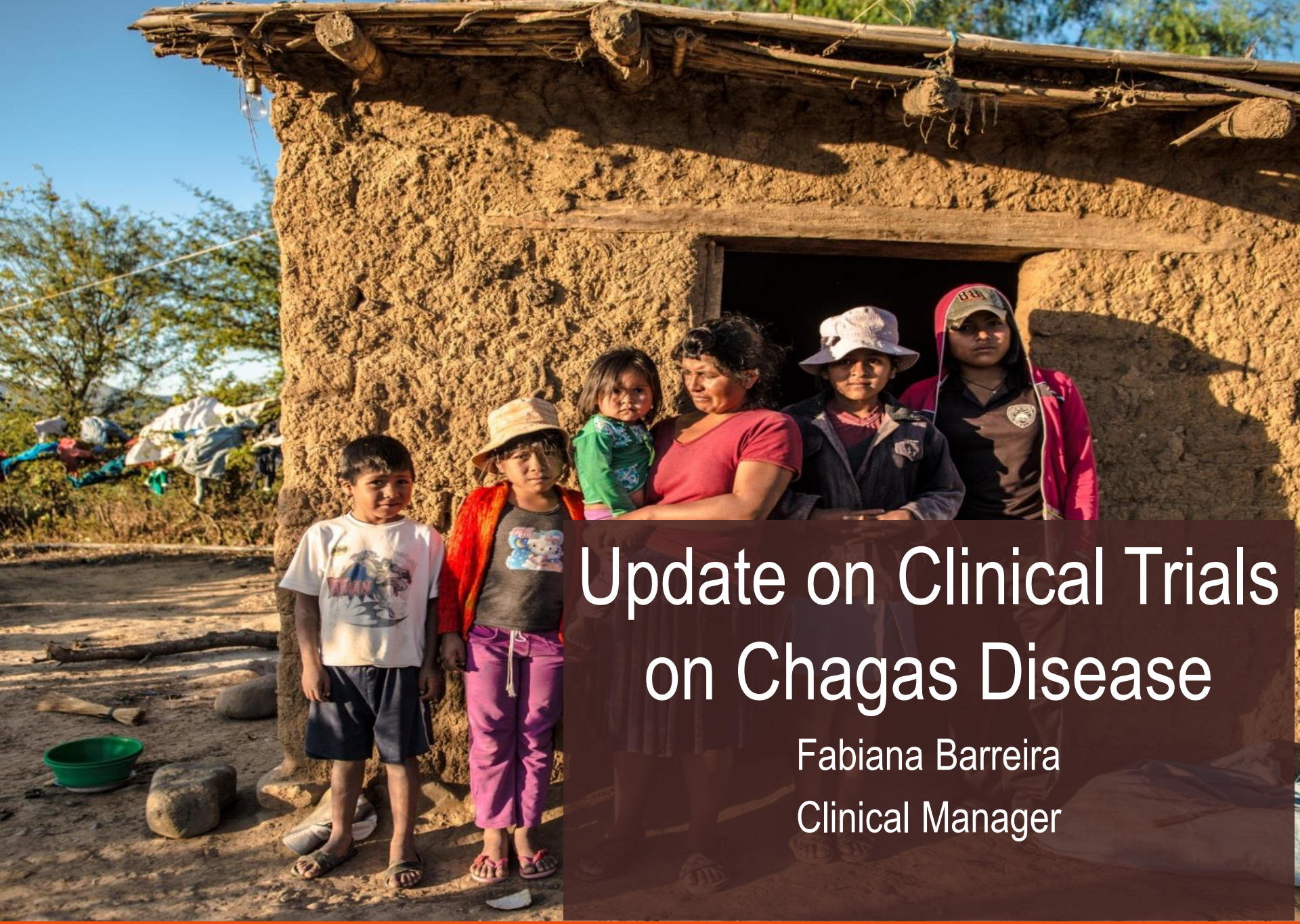
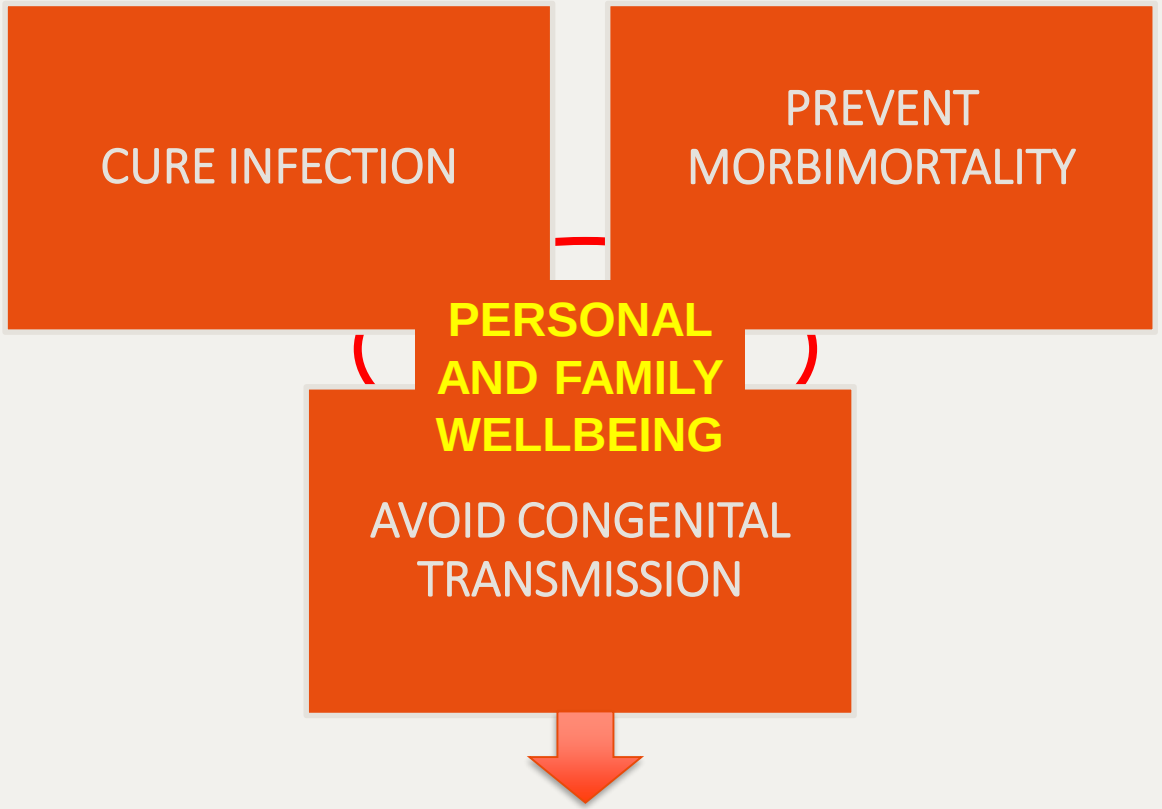


Update on Clinical Trials on Chagas Disease

Fabiana Barreira

Clinical Manager

DIAGNOSIS AND TREATMENT



Chagas Disease – Target Product Profile 2015

	Acceptable	Ideal
Target population	Chronic indeterminate	Chronic indeterminate and Acute
Geographic Distribution	All regions	All regions
Efficacy	Non-inferior to benznidazole standard dose* in all parasitological areas	Superior to benznidazole standard dose in different phases of disease (acute and chronic) (parasitological)
Safety	Superior to benznidazole* in the frequency of definitive treatment discontinuations due to medical indication (clinical and laboratory)**	Superior to benznidazole* in the frequency of definitive treatment discontinuations due to medical indication (clinical and laboratory)**
Contraindications	Pregnancy	No contraindications
Precautions	No genotoxicity**; no pro-arrythmic potential	No genotoxicity; no teratogenicity; no pro-arrythmic potential
Interactions	No clinically significant interaction with anti-arrythmic and anticoagulant drugs	No clinically significant interaction with other drugs
Presentation	Oral/Parenteral (short POC)*** Age-adapted	Oral Age-adapted
Stability	3 years, climatic zone IV	5 years, climatic zone IV
Dosing regimen	Oral - any duration Parenteral - <7 days	<30days
Cost	Lowest possible	≤ current treatment cost

* As per WHO recommendation; ** No genotoxicity is a condition only for NCEs; *** Need for parenteral treatment for severe disease

TRIAZOLES x BZN

Phase II Clinical Trials	CHAGASAZOL *Molina I et al. NEJM 2014;370:1899*	STOP-CHAGAS *Morillo C. et al J Am Coll Cardiol. 2017 ; 69(8)*	PROOF-OF-CONCEPT of E1224
Number of patients	78 (3 groups of 26 patients)	120 (4 groups of 30 patients)	230 (5 groups of 46 patients)
Inclusion criteria	Age ≥ 18; two positive serologic tests; positive rt-PCR	Age 18-50; ≥ 2 positive serologic tests; positive rt-PCR; normal ECG & echo	Age 18-50; ≥ 2 positive serologic tests; positive rt-PCR; normal ECG
Study treatments	-BZN: 150 mg BID -POS: 100 mg BID (low dose) -POS: 400 mg BID (high dose) *For 60 days*	-PCBpos: 10 ml BID -POS: 400 mg (10 ml) BID -BZN 200 mg + PCBpos 10 ml BID -BZN 200 mg + POS 400 mg (10 ml) BID *For 60 days*	-PCB (8w) -E1224 low dose (8w) -E1224 high dose (8w) -E1224 (4w) followed by PCB (4w): short dose -BZN (5mg/kg/d/60d)
Primary end point	Consistently negative results of rt-PCR over the entirely FU period (8, 16, 24, and 40 weeks after EOT)	Consistently negative results of rt-PCR over the entirely FU period (4, 8, 12, and 16 weeks after EOT)	Consistently negative results of rt-PCR at EOT and until 12 months of FU (4, 6 and 12 months)
Population	Patients from Bolivia living in Spain	Patients from ARG (77%), CHILE or LA living in Spain	Patients from Bolivia (Tarija & Cochabamba)

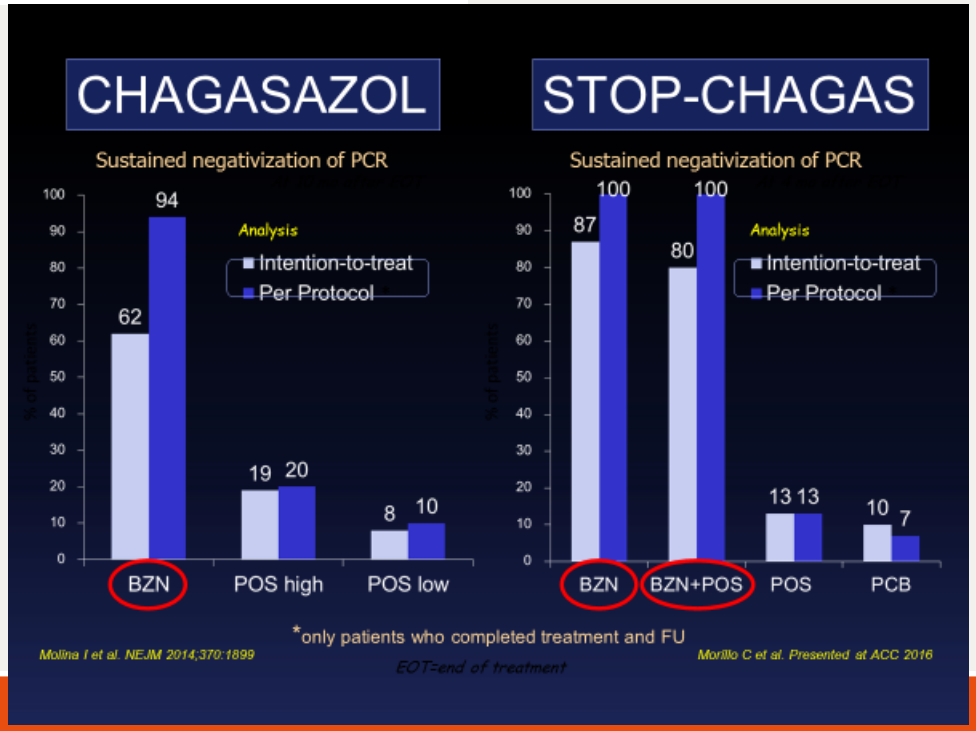
CHAGASAZOL & STOP-CHAGAS

Randomized Trial of Posaconazole and Benznidazole for Chronic Chagas' Disease

Israel Molina, M.D., Jordi Gómez i Prat, M.D., Fernando Salvador, M.D., Begoña Treviño, M.D., Elena Sulleiro, M.D., Núria Serre, M.D., Diana Pou, M.D., Sílvia Roure, M.D., Juan Cabezos, M.D., Lluís Valerio, Ph.D., Albert Blanco-Grau, M.D., Adrián Sánchez-Montalvá, M.D., Xavier Vidal, Ph.D., and Albert Pahissa, Ph.D.

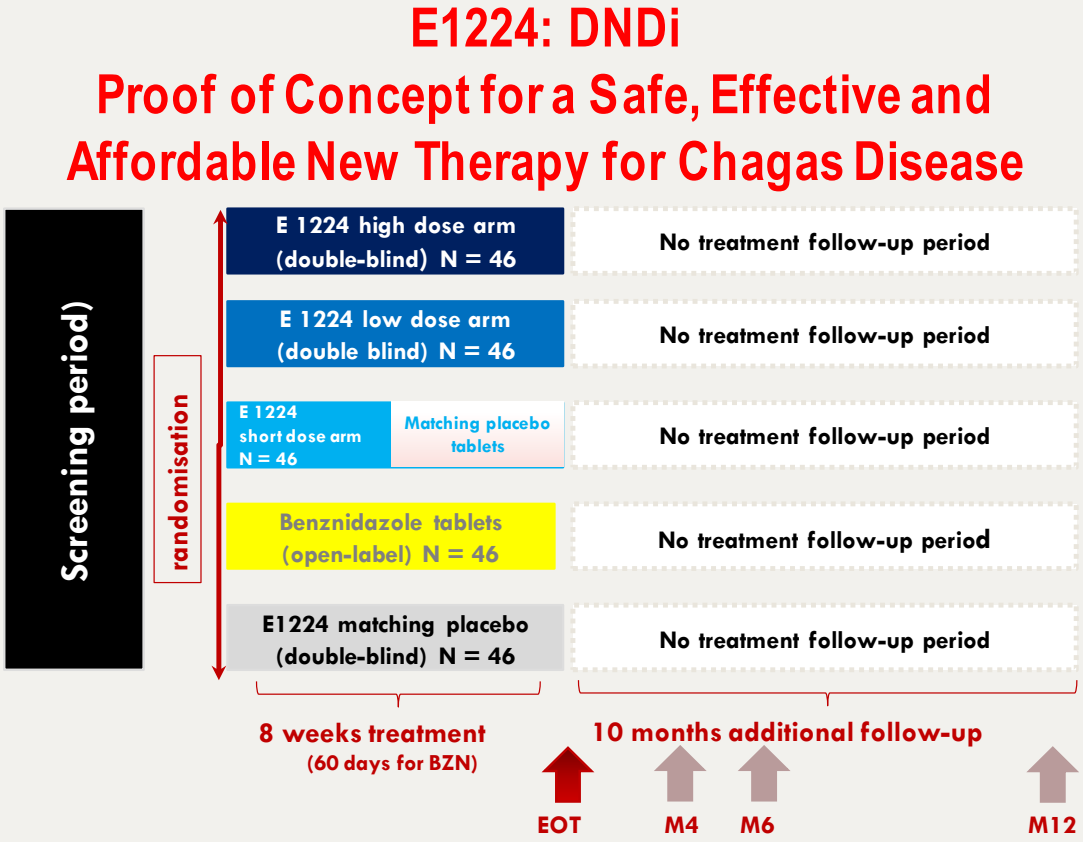
Benznidazole and Posaconazole in Eliminating Parasites in Asymptomatic *T. Cruzi* Carriers

The STOP-CHAGAS Trial



E1224-001

- E1224, Phase 2, Proof of concept

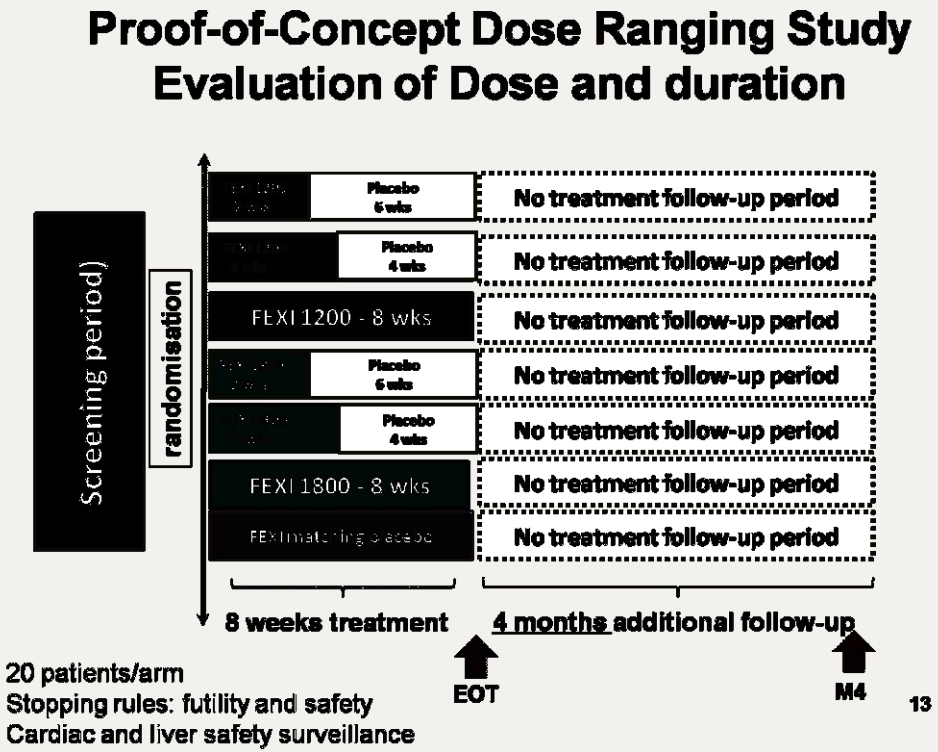


FEXINIDAZOL

- Phase 2, Proof of concept:

Fexnidazole Phase II

DNDi

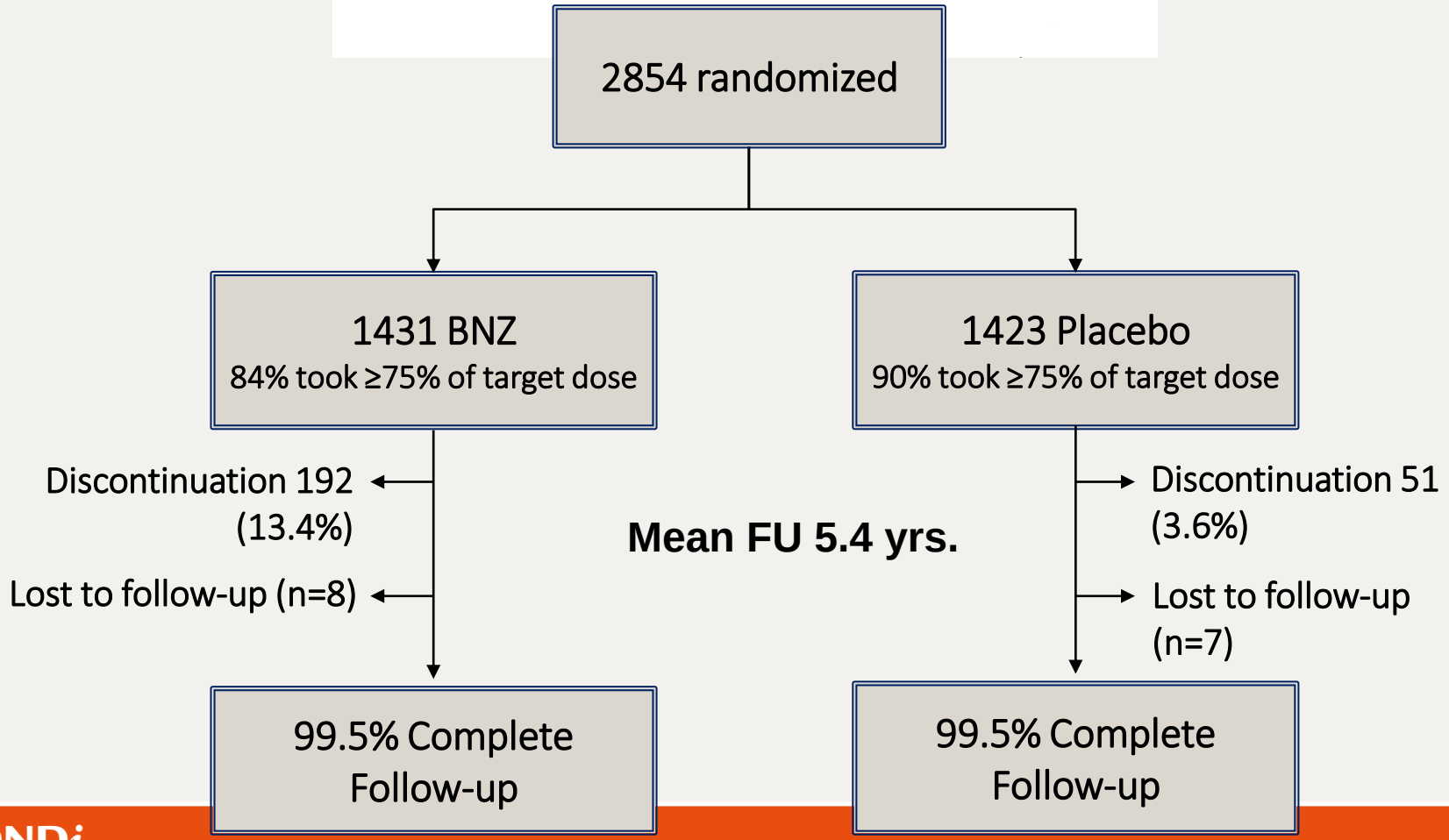


BENEFIT

ORIGINAL ARTICLE

Randomized Trial of Benznidazole for Chronic Chagas' Cardiomyopathy

C.A. Morillo, J.A. Marin-Neto, A. Avezum, S. Sosa-Estani, A. Rassi, Jr., F. Rosas, E. Villena, R. Quiroz, R. Bonilla, C. Britto, F. Guhl, E. Velazquez, L. Bonilla, B. Meeks, P. Rao-Melacini, J. Pogue, A. Mattos, J. Lazdins, A. Rassi, S.J. Connolly, and S. Yusuf, for the BENEFIT Investigators*



NEW SCHEME INTERMITTENT BZN

- Pilot study to assess an intermittent scheme of BZN
- 5mg/kg/day, two daily doses every 5 days, 60 days

AMERICAN SOCIETY FOR MICROBIOLOGY | Antimicrobial Agents and Chemotherapy

New Scheme of Intermittent Benznidazole Administration in Patients Chronically Infected with *Trypanosoma cruzi*: a Pilot Short-Term Follow-Up Study with Adult Patients

María Gabriela Álvarez,[a] Yolanda Hernández,[b] Graciela Bertocchi,[a] Marisa Fernández,[b] Bruno Lococo,[a] Juan Carlos Ramírez,[c] Carolina Cura,[b] Constanza Lopez Albizu,[b] Alejandro Schijman,[c] Marcelo Abril,[d] Sergio Sosa-Estani,[b] Rodolfo Viotti[a]

Hospital Interzonal General de Agudos Eva Perón, San Martín, Buenos Aires, Argentina[a]; Instituto Nacional de Parasitología Dr. Mario Fatala Chaben, Buenos Aires, Argentina[b]; Instituto de Ingeniería Genética y Biología Molecular (INGEBI), Buenos Aires, Argentina[c]; Fundación Mundo Sano, Buenos Aires, Argentina[d]

BERENICE


partners
BERENICE is a European research network (Collaborative Project) coordinated by Vall d' Hebron University Hospital and its Research Institute (ICS-HUVH, Barcelona, Spain). Our consortium brings together 8 European and Latin American partners. Starting in September 2012, this 5-year project is supported by the European Commission under the Health Innovation Work Programme of the 7th Framework Programme.
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For further information, please visit our website at:
www.berenice-project.eu
berenice
BERENICE (Benznidazol and Triazol REsearch group for Nanomedicine and Innovation on Chagas diseasE)
Making possible the treatment of Chagas disease
BERENICE is an European research network (Collaborative Project supported by the European Comision under the Health Innovation Work Programme of the 7th Framework Programme).

SUMMARY OF RECENT RCTs

- Posaconazole (monotherapy or in combination) and E1224 (monotherapy) were effective during treatment and relapsed after EOT (demonstrated by PCR Positive)

- Fexinidazole (suspended for safety issues) was effective during treatment with sustained response (100%) at 12 months FUP

- Benznidazole was effective during treatment with sustained response (~ 80%) at 12 months FUP

- PCR proved useful for assessing treatment response to anti-trypanosomal drugs

THANK YOU

https://www.dndi.org/