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BENznidazole Evaluation For Interrupting Trypanosomiasis pilot trial

Submission date	Recruitment status	[_] Prospectively registered
01/06/2007	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
01/06/2007	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
03/09/2015	Infections and Infestations	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
MCT-79704

Study information

Scientific Title
BENznidazole Evaluation For Interrupting Trypanosomiasis pilot trial

Acronym
BENEFIT Pilot

Study objectives
Benznidazole is effective in producing parasitic cure in patients with Chronic Chagas Cardiomyopathy. 60 days of therapy with Benznidazole will:
1. Increase negativization of Trypanosomiasis cruzi as detected by Polymerase Chain Reaction (PCR) by at least 30%, and
2. Reduce t. cruzi parasite load by at least 50%

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Research Ethics Board of Hamilton Health Sciences Corporation & McMaster University (Canada), 21/09/2006, ref: NREC # 05-348
2. Comité de Ethica em Pesquisa de l'Hospital das Clinicas da Faculdade de Medicina de Ribeirao Preto da Universidade de Sao Paulo (Brazil), 04/02/2004, ref: NREC# 213/2004
3. Ministerio de Salud y Ambiente (Argentina), 11/03/2005, ref: NREC 1-0047-0000-00733-05-1
4. Comite Investigaciones de Fundacion ABBOD SHAIO (Columbia), 19/04/2004

Study design
Multicentre multinational two-arm randomised parallel controlled placebo trial with study participant, study investigator, caregiver, outcome assessor, and data analyst blinding

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Chagas disease; American trypanosomiasis

Interventions
1. Benznidazole: 60 days of treatment at 5 mg/kg/day given twice a day (at maximum dose of 400 mg/day)
2. Matching placebo: 60 days of treatment at 5 mg/kg/day given twice a day (at maximum dose of 400 mg/day)

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Benznidazole

Primary outcome(s)

There are two related co-primary outcomes:
1. Negativisation and reduction of t. cruzi detected by PCR at the end of treatment which lasted 60 days, and at a two-year follow-up
2. Reduction in the mean burden of t. cruzi (parasite load) as detected by the concentration of t. cruzi/ml of blood by PCR in the treated group, at the end of treatment which lasted 60 days, and at a two-year follow-up

Key secondary outcome(s))
1. Safety and tolerability of benznidazole in chronic Chagas cardiomyopathy, 11 ± 2 days after initial randomisation, three weeks ± 3 days after randomisation, end of therapy (60 days) and two years later
2. Long-term feasibility of conducting a Randomised Controlled Trial (RCT) in patients with Chagas disease measured by patient enrolment and completion of follow-up, recruitment rate measured at baseline, completion measured at the end of therapy (60 days later), and two years later
3. Cardiovascular events:
3.1. Composite of major cardiovascular outcomes defined as the first occurrence of: death, cardiac arrest, sustained ventricular tachycardia, symptomatic heart failure, pacemaker or implantable cardiac defibrillator insertion, ischemic stroke or other systemic thromboembolic event, 11 days, 21 days, 60 days, 6 months, 1 year and 2 year after randomisation
3.2. New development of any of the following echo changes: segmental wall motion abnormalities, ventricular aneurysm, reduction in LV ejection fraction greater than 5%, increase in Left Ventricular end-Diastolic Dimension [LVDD] greater than 5.0 mm compared with baseline, 11 days, 21 days, 60 days, 6 months, 1 year and 2 year after randomisation
3.3. New 12 lead ECG alterations (complete bundle branch block, fascicular block, advanced atrio-ventricular block, atrial fibrillation, etc); 1st Degree AV Block PR greater than 280 ms, 11 days, 21 days, 60 days, 6 months, 1 year and 2 year after randomisation
3.4. Progression of NYHA functional class by at least one category, 11 days, 21 days, 60 days, 6 months, 1 year and 2 year after randomisation

Completion date
30/04/2009

Eligibility

Key inclusion criteria
1. Either sex, aged greater than or equal to 18 and less than or equal to 70 years
2. At least two positive serological tests for Chagas disease (indirect immunofluorescence, indirect hemagglutination, OR Enzyme-Linked Immunosorbent Assay [ELISA]) and at least ONE of the following markers of cardiac involvement (which identify individuals at high risk of progression):
2.1. Abnormal 12 lead Electrocardiogram (ECG): One-major criteria (second or third degree AV block) OR at least two minor criteria:
2.1.1. Any bundle branch block
2.1.2. Any fascicular block
2.1.3. Ventricular premature beats (greater than one)
2.1.4. First degree AV block greater than 220 ms, in the absence of drugs that slow AV node conduction
2.1.5. Mobitz type I AV block, in the absence of drugs that slow AV
2.1.6. Sinus bradycardia less than 50 bpm or sinus pauses greater than 3.0s, in the absence of sinus node blocking drugs

2.1.7. Low voltage of QRS in the frontal plane
2.1.8. Atrial fibrillation
2.2. Increased cardiothoracic ratio greater than 0.50 at baseline on upright chest X ray
2.3. Evidence of regional wall motion abnormality (hypokinesis, akinesis or dyskinesis) or reduced global Left Ventricular Systolic Function (LVEF) less than 50% (2D-Echo Radionuclide Angiography [RNA] LV ventriculography) or increased left ventricular diastolic diameter (greater than 55 mm) on 2D-Echo
2.4. Complex ventricular arrhythmias (multiform greater than 10/hour, couplets or non-sustained Ventricular Tachycardia [NSVT]) on 24 hour ambulatory ECG monitoring

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. New York Heart Association (NYHA) heart failure class IV or decompensated heart failure
2. Evidence of concomitant Coronary Artery Disease (CAD) or other etiology of dilated cardiomyopathy
3. Previous treatment with antitrypanosomal agents or an accepted indication for antiparasitic therapy (e.g. reactivation of Chagas infection due to immunosuppression by several diseases or treatment with steroids)
4. Patients living in inadequate housing conditions that may predispose to t. cruzi re-infection will not be excluded; instead this condition will be appropriately documented
5. Inability to comply with follow-up
6. History of severe alcohol abuse within two years
7. Known chronic renal insufficiency (serum creatinine greater than 2.5 mg/dl or 200 umol) or hepatic insufficiency (Aspartate Aminotransferase [AST]/Alanine Aminotransferase [ALT] greater than 3 x normal)
8. Pregnancy or breast feeding
9. Megaesophagus with swallowing impairment
10. Other severe disease significantly curtailing life expectancy

Date of first enrolment
01/03/2006

Date of final enrolment
30/04/2009

Locations

Countries of recruitment
Argentina

Brazil

Canada

Colombia

Study participating centre
McMaster University
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Sponsor information

Organisation
Hamilton Health Science Corporation (HHSC) (Canada)

ROR
https://ror.org/02dqdxm48

Funder(s)

Funder type
Research organisation

Funder Name
The Canadian Institutes of Health Research (CIHR) (Canada) - http://www.cihr-irsc.gc.ca (ref: MCT-79704)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/10/2015		Yes	No
Protocol article	protocol	01/07/2008		Yes	No