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TNT-1:OPTIMA (Tri-National Trial 1: Options in Management with Anti-retrovirals) - A tri-national (Canada, UK, USA) randomised controlled trial to determine the optimal management of patients with Human Immunodeficiency Virus (HIV) infection for whom first and second-line Highly Active Anti-Retroviral Therapy (HAART) has failed

Submission date 19/01/2001	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 19/01/2001	**Overall study status** Completed	
Last Edited 21/03/2016	**Condition category** Infections and Infestations	

Plain English summary of protocol
Not provided at time of registration

Study website
http://www.optimatrial.org/ca/

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number
NCT00050089

Secondary identifying numbers
JTN-43304; G9901441

Study information

Scientific Title
TNT-1:OPTIMA (Tri-National Trial 1: Options in Management with Anti-retrovirals) - A tri-national (Canada, UK, USA) randomised controlled trial to determine the optimal management of patients with Human Immunodeficiency Virus (HIV) infection for whom first and second-line Highly Active Anti-Retroviral Therapy (HAART) has failed

Acronym
OPTIMA

Study objectives
The OPTIMA trial is a large-scale, multicentre, randomised controlled trial to compare the relative efficacy of two different therapeutic strategies:
1. A drug free period
2. Increasing the number of HIV drugs in treating HIV infection after the most effective drug combinations have failed.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ottawa Hospital Research Ethics Board, 20/11/2001

Study design
Randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Not specified

Study type(s)
Treatment

Participant information sheet
Patient information can be found at: http://www.optimatrial.org/ca/pdfs/brochure.pdf

Health condition(s) or problem(s) studied
HIV, Acquired Immune Deficiency Syndrome (AIDS)

Interventions
1. Start a standard-ART regimen (up to four HIV drugs)
2. Start a mega-ART regimen (five or more HIV drugs)
3. Interrupt ART for 12 weeks then start a standard-ART regimen (up to four HIV drugs)
4. Interrupt ART for 12 weeks then start a mega-ART regimen (five or more HIV drugs)

Added as of 07/02/2007 for UK part of trial:
You can now join this study in the UK in one of three ways:
Option 1: As in the main OPTIMA study, you will be randomised (similar to tossing a coin or rolling a dice) to both parts of the study. You will have a drug-free period of three months, or no drug-free period and then receive either 'standard ART' or 'mega-ART treatment.
Option 2: You can choose whether or not to have a drug free period, and then be randomised for how many drugs you will take.
Option 3: You can choose how many drugs you will take, and then be randomised to whether you will have a drug free period or not.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Anti-retroviral therapy

Primary outcome measure
The time to new or recurrent AIDS-defining event or death and time to a new non-HIV related serious adverse event are main clinical outcomes.

Secondary outcome measures
1. Time to development of a new non-HIV related serious adverse event
2. Quality of life
3. Incidence of grade 3 or 4 clinical or laboratory adverse events
4. Changes in CD4 counts, viral load and resistance
5. Process measures including hematologic profiles, electrolytes, renal function, liver function and pancreatic function

Overall study start date

01/01/2002

Completion date
01/12/2007

Eligibility

Key inclusion criteria
1. Signed informed consent
2. Age 18 years or more, either sex
3. HIV-1 infection confirmed by Enzyme-Linked Immuno-Sorbent Assay (ELISA) or Western Blot or detectable HIV viral load at any time
4. Failure of at least two different multi-drug regimens, which included drugs of all classes that the patient can tolerate
5. At least 3 months continuous HAART and still on treatment
6. Two most recent results (can include screening) on current Anti-Retroviral Therapy (ART) of either:
6.1. CD4 less than 100 plus plasma Viral Load (pVL) greater than 5000 copies, or
6.2. CD4 100 - 199 plus pVL greater than 10,000 copies

*If VL testing available defined as either: failure to suppress pVL after 24 weeks of therapy, or rebound of at least 0.5 log10 in pVL from the nadir. In the era before pVL available defined as: a decline in the CD4 count over 50% from the peak, or progression of HIV disease.

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
504 (as of 07/02/2007: 390)

Key exclusion criteria
1. Pregnancy, breast-feeding or planned pregnancy
2. Likelihood of poor protocol follow-up or if Mega-ART is not feasible (due to significant intolerance of many ART drugs)
3. Serious, uncontrolled major opportunistic infection (OI) within 14 days of screening
4. Likelihood of early death due to non HIV-disease
5. Any medical condition or current medication, in the opinion of the treating physician, which would contraindicate anti-HIV treatment as allocated in the trial

Exclusion criteria for UK arm of trial added as of 07/02/2007:
1. Pregnancy, breast-feeding or planned pregnancy

2. Likelihood of poor protocol follow-up or if Mega-ART is not feasible* (due to significant intolerance of many ARV rugs)
3. Serious, uncontrolled major opportunistic infection (OI) within 14 days of screening
4. Likelihood of early death due to non-HIV disease
*Patients exempt from second part of this question if entering option 3

Date of first enrolment
01/01/2002

Date of final enrolment
01/12/2007

Locations

Countries of recruitment
Canada

United Kingdom

United States of America

Study participating centre
The Ottawa Hospital - General Campus
Ontario
Canada
K1H 8L6

Sponsor information

Organisation
University of British Columbia (Canada)

Sponsor details
2075 Wesbrook Mall
Vancouver
Canada
V6T 1Z1

Sponsor type
University/education

Website
http://www.ubc.ca/

Organisation
Medical Research Council (MRC) Clinical Trials Unit (UK)

Sponsor details
222 Euston Road
London
United Kingdom
NW1 2DA

Sponsor type
Research council

Website
www.ctu.mrc.ac.uk

Organisation
University of British Columbia

Sponsor details

Sponsor type
Not defined

Website
https://www.ubc.ca/

ROR
https://ror.org/03rmrcq20

Funder(s)

Funder type
Research organisation

Funder Name
Canadian Institutes of Health Research (ref: JTN-43304)

Alternative Name(s)
Instituts de Recherche en Santé du Canada, Canadian Institutes of Health Research (CIHR), CIHR_IRSC, Canadian Institutes of Health Research | Ottawa ON, CIHR, IRSC

Funding Body Type
Government organisation

Funding Body Subtype

National government

Location
Canada

Funder Name
Medical Research Council (UK) (ref: G9901441)

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

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?
Basic results				No	No
Protocol article	protocol	01/08/2003		Yes	No
Results article	quality of life results	15/08/2009		Yes	No
Results article	mutation frequency results	01/06/2010		Yes	No
Results article	results	31/03/2011		Yes	No