New Era Study: Treatment With Multi Drug Class (MDC) HAART in HIV Infected Patients (NewEra)

ClinicalTrials.gov Identifier: NCT00908544

Recruitment Status : Completed
First Posted : May 27, 2009
Results First Posted : August 26, 2019
Last Update Posted : August 26, 2019

Sponsor:
MUC Research GmbH

Collaborators:
Merck Sharp & Dohme Corp.
AbbVie
Pfizer
German Center for Infection Research

Information provided by (Responsible Party):
MUC Research GmbH

Study Description

Go to

Brief Summary:

This is a multi-center, open-label, non-randomized proof-of-concept trial. Two cooperating HIV-specialized centres represented by Dr. med. Hans Jaeger and Prof. Dr. Johannes Bogner are planning to perform an IIT (investigator initiated trial) with the goal to eradicate HIV in N=40 HIV-infected patients with either primary infection or chronic infection and successful HAART (Highly Active Antiretroviral Treatment) of several years.

All patients will be started on a multi-drug HAART including two Nucleoside-Reverse-Transcriptase-Inhibitors (NRTI´s), one Protease-Inhibitor (PI), a CCR5-inhibitor and an Integrase-Inhibitor (INI). Decay of viral reservoirs like latently HIV-infected CD4+ T-cells will be monitored over time.

Condition or disease	Intervention/treatment	Phase
HIV Infections	Other: PHI-patients Other: CHI-patients	Not Applicable

Show Detailed Description

Study Design

Go to

Study Type :	Interventional (Clinical Trial)
Actual Enrollment :	47 participants
Allocation:	Non-Randomized
Intervention Model:	Parallel Assignment
Masking:	None (Open Label)
Primary Purpose:	Treatment
Official Title:	NEW ERA STUDY - HIV and Eradication: A Multicenter, Open-label, Non-randomized Trial to Evaluate Treatment With Multi-drug Class (MDC) HAART and Its Impact on the Decay Rate of Latently Infected CD4+ T Cells Incl. Amendment 1.0
Actual Study Start Date :	May 15, 2009
Actual Primary Completion Date :	April 3, 2018
Actual Study Completion Date :	May 2018

Resource links provided by the National Library of Medicine

MedlinePlus related topics: HIV/AIDS

U.S. FDA Resources

Arms and Interventions

Go to

Arm	Intervention/treatment
Experimental: PHI-patients Patients with primary HIV infection (PHI) (see also "Eligibility") are immediately treated with 2 NRTI + 1 PI/r + Maraviroc + Raltegravir	Other: PHI-patients Treatment initiation with multi drug class (MDC) HAART. 2

	NRTI + 1 PI/r + Maraviroc + Raltegravir
Experimental: CHI-patients Patients with chronic HIV infection (CHI) and with suppressed plasma viral load for at least three years under continuous HAART (2 NRTI + 1 PI/r see also "Eligibility") intensified by Maraviroc + Raltegravir	Other: CHI-patients Treatment intensification of PI-based HAART with Maraviroc and Raltegravir. 2 NRTI + 1 PI/r + Maraviroc + Raltegravir

Outcome Measures

Go to

Primary Outcome Measures :

1. Combined Endpoint Including HIV RNA and HIV DNA [Time Frame: Screening, month -3 (= pre-baseline only for CHI-patients), baseline, months 1, 3, 6 and then every 6 months until month 84]

   The primary outcome measure (i.e. achievement of 'eradication') is a combined endpoint including cell-associated proviral DNA and plasma HIV RNA and is defined as undetectable cell-associated HIV DNA (copies per 10exp6 PBMC (peripheral blood mononuclear cells) and per 10exp6 CD4 cells) for at least 2 years (measurement by the French ANRS Group) combined with plasma viral load < 50 copies/ml for at least 5 years and undetectable plasma viral load (HIV RNA < 1 copy/ml, 1-copy assay) for at least 2 years.

Secondary Outcome Measures :

1. Mean Change in HIV DNA in PBMC (Month 36 and Month 84) [Time Frame: Change from baseline at months 36 and 84]

   Mean change (CI=95% Confidence Intervall) in HIV DNA copies/10exp6 PBMC (= peripheral blood mononuclear cells) from baseline, to evaluate the decay rates of latently infected cell reservoir.

2. Mean Change in HIV DNA in CD4+T Cells (Month 36 and Month 84) [Time Frame: Change from baseline at months 36 and 84]

   Mean change (CI=95% Confidence Intervall) in HIV DNA copies/10exp6 CD4+T cells from baseline, to evaluate the decay rates of latently infected cell reservoir.

3. HIV RNA <50 Copies/ml (Proportion) [Time Frame: Baseline and at months 1, 3, 6 and then every 6 months until month 84]

   Percentage of patients with Plasma HIV RNA <50 copies/ml at baseline and during follow-up

4. Median Change in HIV DNA in PBMC Over Time [Time Frame: Change from baseline at months 1, 3, 6 and then every 6 months until month 84]

   Median Change from baseline (IQR, interquartile range) in HIV DNA copies/10exp6 PBMC (= peripheral blood mononuclear cells), to evaluate the decay rates of latently infected cell reservoir.

5. Median Change in HIV DNA in CD4+T Cells Over Time [Time Frame: Change from baseline at months 1, 3, 6 and then every 6 months until month 84]

   Median Change from baseline (IQR, interquartile range) in HIV DNA in CD4+T cells, to evaluate the decay rates of latently infected cell reservoir.

6. Median Change in CD4+T Cells Over Time [Time Frame: Change from baseline at months 1, 3, 6 and then every 6 months until month 84]

   Median Change from baseline (IQR, interquartile range) in CD4+T cells/µl.

7. Median Change in Relative CD4+T Cells Over Time [Time Frame: Change from baseline at months 1, 3, 6 and then every 6 months until month 84]

   Median Change from baseline (IQR, interquartile range) in relative CD4+T cells/µl.

8. Median Change in CD4+/CD8+ Ratio Over Time [Time Frame: Change form Baseline at months 1, 3, 6 and then every 6 months until month 84]

   Median change in CD4+/ CD8+ ratio at baseline (IQR, interquartile range) and during follow-up

9. Median Change in CD8+T Cells Over Time [Time Frame: Change from baseline at months 1, 3, 6 and then every 6 months until month 84]

   Median Change from baseline (IQR, interquartile range) in CD8+T cells/µl.

10. Median Change in CD8+CD38+T Cells Over Time [Time Frame: Change from baseline at months 1, 3, 6 and then every 6 months until month 84]

    Median Change from baseline (IQR, interquartile range) in CD8+CD38+T cells/µl.

11. Absolute HIV DNA in PBMC [Time Frame: Baseline and at months 1, 3, 6 and then every 6 months until month 84]

    Absolute HIV DNA in PBMC (= peripheral blood mononuclear cells) from baseline (Median; IQR, interquartile range), to quantify the cell-associated latently infected reservoir size by visit and treatment Group.

12. Absolute HIV DNA in CD4+T Cells [Time Frame: Baseline and at months 1, 3, 6 and then every 6 months until month 84]

    Absolute HIV DNA in CD4+T cells from baseline (Median; IQR, interquartile range), to quantify the cell-associated latently infected reservoir size by visit and treatment Group.

13. Absolute CD4+T Cells [Time Frame: Baseline and at months 1, 3, 6 and then every 6 months until month 84]

    Median CD4+T cells/µl at baseline (IQR, interquartile range) and during follow-up

14. Relative CD4+T Cells [Time Frame: Baseline and at months 1, 3, 6 and then every 6 months until month 84]

    Median relative CD4+T cells/µl at baseline (IQR, interquartile range) and during follow-up

15. CD4+/CD8+ Ratio [Time Frame: Baseline and at months 1, 3, 6 and then every 6 months until month 84]

    Median CD4+/CD8+ ratio at baseline (IQR, interquartile range) and during follow-up

16. Absolute CD8+T Cells [Time Frame: Baseline and at months 1, 3, 6 and then every 6 months until month 84]

    Median CD8+T cells/µl at baseline (IQR, interquartile range) and during follow-up

17. Absolute CD8+CD38+T Cells [Time Frame: Baseline and at months 1, 3, 6 and then every 6 months until month 84]

    Median CD8+CD38+T cells/µl at baseline (IQR, interquartile range) and during follow-up

Eligibility Criteria

Go to

Information from the National Library of Medicine

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the contacts provided below. For general information, Learn About Clinical Studies.

Ages Eligible for Study:	18 Years to 70 Years (Adult, Older Adult)
Sexes Eligible for Study:	All
Accepts Healthy Volunteers:	No

Criteria

1. Inclusion Criteria:

   For all patients:

   - HIV-infected patient
   - Age greater 18 years
   - No acute AIDS-defining disease or history of AIDS- defining disease
   - CD4-cell nadir above or equal 200 cells/µL
   - Hemoglobin greater 8 g/dl
   - Neutrophil count greater 750 cells/µL
   - Platelet count greater 50.000 cells/µL
   - AST/ALT below 5x upper limit of normal range
   - No evidence for drug intolerability
   - No prior use of an HIV integrase inhibitor or CCR5 antagonist
   - No presence of malignancy (requiring active treatment and malignancy within 5 years prior to enrolment (even if in complete remission)
   - No significant underlying disease (non-HIV) that might impinge upon disease progression or death
   - No history of alcohol or other substance abuse or other condition which in the opinion of the investigator would interfere with the patient compliance or safety.
   - Written informed consent
   - For males and premenopausal females use of acceptable methods of birth control during the entire study and for 6 weeks thereafter
   - No pregnancy (for premenopausal women: negative serum or urine pregnancy test within 48 hours prior to initiating study medications)
   - No breastfeeding

   For chronically HIV-infected patients (CHI):

   - Continuous plasma viral load below 50 copies/ml for the preceding 36 months under HAART (two or less single viral load blips up to 500 copies/ml are allowed)
   - Stable HAART (for at least 3 months) prior to the Screening visit consisting of 2 NRTI + 1 PI
   - No history of virological failure
   - No documented resistance to PI and NRTI
   - CCR5-tropic virus

For patients with primary HIV infection (PHI):

- Detectable plasma viral load
- ELISA positive or negative and Western Blot negative or positive with less or equal 2 bands at screening visit
- No primary resistance to PI´s and NRTI´s
- CCR5-tropic virus

2. Exclusion criteria:

Evidence for drug intolerability or contraindication concerning any drug foreseen for MDC HAART

- Documented HIV-1 resistance to PI and/or NRTI.
- CD4 nadir <200/µL
- Acute AIDS-defining disease or history of AIDS-defining disease
- CHI: preceding virological failure
- History of alcohol or other substance abuse or other condition which in the opinion of the investigator would interfere with the patient compliance or safety.
- Any of the following abnormal laboratory test results in screening:
  1. Hemoglobin < 8 g/dL
  2. Neutrophil count < 750 cells/µL
  3. Platelet count < 50,000 cells/µL
  4. AST or ALT > 5x the upper limit of normal
- Presence of malignancy (requiring active treatment and malignancy within 5 years prior to enrolment (even if in complete remission)
- Significant underlying disease (non-HIV) that might impinge upon disease progression or death
- Prior use of any experimental HIV- Integrase-Inhibitor or CCR5-antagonist.
- Patient is pregnant or breastfeeding, or expecting to conceive (within the duration of the study). Patient is expecting to donate eggs (within the duration of the study). Patient is expecting to donate sperm (within the duration of the study).
- Contraindications for Maraviroc (Celsentri®) or Raltegravir (Isentress®) according to the respective summary of product characteristics (see also product informations attached to the protocol) (Hypersensitivity to the active substances or any of the excipients).

Contacts and Locations

Go to

Information from the National Library of Medicine

To learn more about this study, you or your doctor may contact the study research staff using the contact information provided by the sponsor.

Please refer to this study by its ClinicalTrials.gov identifier (NCT number): ***NCT00908544***

Locations

Germany

Onkology Karlsruhe
Karlsruhe, Baden-Wuerttemberg, Germany, 76135

Private Practice for Internal Medicine, Hematology and Oncology
Mannheim, Baden-Wuerttemberg, Germany, 68161

Private Practice Drs Ulmer/Frietsch/Mueller
Stuttgart, Baden-Wuerttemberg, Germany, 70197

Practice Dr. med. Lothar Schneider
Fürth, Bavaria, Germany, 90762

Private Practice Drs Pauli/Becker
Munich, Bavaria, Germany, 80331

MVZ Karlsplatz
Munich, Bavaria, Germany, 80335

University Munich University Hospital, Dept. of Infectious Diseases
Munich, Bavaria, Germany, 80336

ICH Study Center
Hamburg, Germany, 20354

Sponsors and Collaborators

MUC Research GmbH

Merck Sharp & Dohme Corp.

AbbVie

Pfizer

German Center for Infection Research

Investigators

Study Chair:	Hans Jaeger, MD	MUC Research GmbH
Study Chair:	Johannes Bogner, Prof., MD	University Munich, University Hospital, Dept. of Infectiou

Study Documents (Full-Text)

Documents provided by MUC Research GmbH:

Study Protocol and Statistical Analysis Plan [PDF] November 6, 2014

More Information

Go to

Publications of Results:

Grützner EM, Hoffmann T, Wolf E, Gersbacher E, Neizert A, Stirner R, Pauli R, Ulmer A, Brust J, Bogner JR, Jaeger H, Draenert R. Treatment Intensification in HIV-Infected Patients Is Associated With Reduced Frequencies of Regulatory T Cells. Front Immunol. 2018 Apr 30;9:811. doi: 10.3389/fimmu.2018.00811. eCollection 2018.

Other Publications:

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Hütter G, Ganepola S. Eradication of HIV by transplantation of CCR5-deficient hematopoietic stem cells. ScientificWorldJournal. 2011 May 5;11:1068-76. doi: 10.1100/tsw.2011.102.

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Sáez-Cirión A, Bacchus C, Hocqueloux L, Avettand-Fenoel V, Girault I, Lecuroux C, Potard V, Versmisse P, Melard A, Prazuck T, Descours B, Guergnon J, Viard JP, Boufassa F, Lambotte O, Goujard C, Meyer L, Costagliola D, Venet A, Pancino G, Autran B, Rouzioux C; ANRS VISCONTI Study Group. Post-treatment HIV-1 controllers with a long-term virological remission after the interruption of early initiated antiretroviral therapy ANRS VISCONTI Study. PLoS Pathog. 2013 Mar;9(3):e1003211. doi: 10.1371/journal.ppat.1003211. Epub 2013 Mar 14.

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Individual Participant Data (IPD) Sharing Statement:

Plan to Share IPD: No

Keywords provided by MUC Research GmbH:

HIV-infection

Primary HIV-infection

Proviral DNA

Eradication

Multi drug class HAART

Additional relevant MeSH terms:

Infection
HIV Infections
Acquired Immunodeficiency Syndrome
Lentivirus Infections
Retroviridae Infections
RNA Virus Infections
Virus Diseases
Sexually Transmitted Diseases, Viral
Sexually Transmitted Diseases
Immunologic Deficiency Syndromes
Immune System Diseases
Slow Virus Diseases
Raltegravir Potassium
Maraviroc
Anti-HIV Agents
Anti-Retroviral Agents
Antiviral Agents
Anti-Infective Agents
HIV Integrase Inhibitors
Integrase Inhibitors
Enzyme Inhibitors
Molecular Mechanisms of Pharmacological Action
HIV Fusion Inhibitors
Viral Fusion Protein Inhibitors
CCR5 Receptor Antagonists