Trial record **1 of 1** for: Endure (ENDURE-CML-IX)

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ENDURE - Efficacy and Safety of AOP2014 With CML Patients in Remission (ENDURE-CML-IX)

This study is currently recruiting participants.

See Contacts and Locations

Verified April 2017 by *Philipps University Marburg Medical Center*

Sponsor:
Philipps University Marburg Medical Center

ClinicalTrials.gov Identifier:
NCT03117816

First Posted: April 18, 2017
Last Update Posted: August 22, 2017

Collaborators:
Deutsche Krebshilfe e.V., Bonn (Germany)
AOP Orphan Pharmaceuticals AG

Information provided by (Responsible Party):
Philipps University Marburg Medical Center

Full Text View | Tabular View | No Study Results Posted | Disclaimer
How to Read a Study Record

Purpose

A randomized, open-label assessor blinded, multi-center, controlled phase II Trial to evaluate the efficacy of AOP2014 administered bi-weekly subcutaneously (s.c.) in preventing molecular relapse (loss of MMR) in CML patients, who discontinue ABL tyrosine kinase inhibitor therapy (TKI) in deep molecular remission of MR4 or better (MR4.5, or MR5).

Condition	Intervention	Phase
Chronic Myeloid Leukemia in Remission	Drug: AOP2014 / Pegylated-Proline-interferon alpha-2b Other: Surveillance	Phase 2

Study Type: Interventional

Study Design: Allocation: Randomized
Intervention Model: Parallel Assignment
Masking: Single (Outcomes Assessor)
Masking Description:
A randomized, open-label assessor blinded, multi-center, controlled phase II trial
Primary Purpose: Prevention

Official Title: Efficacy and Safety of Pegylated Proline Interferon Alpha 2b (AOP2014) in Maintaining Deep Molecular Remissions in Patients With Chronic Myeloid Leukemia (CML) Who Discontinue ABL-Kinase Inhibitor Therapy - a Randomized Phase II, Multicenter Trial With Post-study Follow-up

Resource links provided by NLM:

Genetics Home Reference related topics: chronic myeloid leukemia

MedlinePlus related topics: Chronic Myeloid Leukemia Leukemia

Drug Information available for: Proline Interferon Interferon Alfa-2b

Genetic and Rare Diseases Information Center resources: Myeloid Leukemia Chronic Myeloid Leukemia Chronic Myeloproliferative Disorders

U.S. FDA Resources

Further study details as provided by Philipps University Marburg Medical Center:

Primary Outcome Measures:

- RFS 7 [Time Frame: Month 7]

  The primary efficacy endpoint is molecular relapse free survival, RFS, at month 7 after randomization. Relapse is defined as loss of major molecular remission, MMR, which is any increase of the BCR-ABL ratio to > 0.1% according to the international scale (IS). Time to relapse is defined as the time from randomization to relapse

Secondary Outcome Measures:

- RFS 13 [Time Frame: Month 13]

  The relapse free survival, RFS, at month 13 after randomization

- RFS 25 [Time Frame: Month 25]

  The relapse free survival, RFS, at month 25 after randomization

- Number of participants with treatment-related adverse events as assessed by CTCAE v4.03 [Time Frame: Day 0 - Month 18]

  Adverse events, serious adverse events (AEs, SAEs)• Safety, tolerability and toxicity based on incidences of adverse events, serious adverse events, frequency of clinical laboratory tests by worst toxicity grade

- Quality of life measured by EORTC QLQ-C30 [Time Frame: Day 0 - Month 18]

  The data will be compared between the treatment groups and to QoL of normal population.

- Quality of life measured by EORTC-QLQ-CML24 [Time Frame: Day 0 - Month 18]

  The data will be compared between the treatment groups and to QoL of normal population. Furthermore, results of the CML24 module should be shared with the EORTC group to complete the validation of this questionnaire

- detection of blood parameter 95 CD86+pDC as RFS predictor [Time Frame: Day 0 - Month 25]

  To validate the value of 95 CD86+pDC / 105 lymphocytes at baseline (before TKI stop) as a predictor of RFS

- OS (overall survival) [Time Frame: Day 0 - Month 25]

  Overall survival (OS), defined as the time between the date of randomization and the date of death from any cause.

Estimated Enrollment:	214
Actual Study Start Date:	May 4, 2017
Estimated Study Completion Date:	December 2024
Estimated Primary Completion Date:	September 2021 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions
Experimental: investigational arm A There will be an overlapping treatment with AOP2014 and TKI for one month. After one month, the TKI therapy will be stopped and patient will receive only AOP2014 treatment for the next 14 months.	Drug: AOP2014 / Pegylated-Proline-interferon alpha-2b AOP2014 as pre-filled auto-injection pen for subcutaneous injection, containing 250 µg AOP2014 / 0.5 ml. The solution also contains inactive ingredients (sodium chloride, polysorbate 80, benzyl alcohol, sodium acetate, and acetic acid). The solution is colorless to light yellow.
surveillance arm B This is an open-label study with a "no treatment/ surveillance" group as comparator arm. Similar as in the arm A, patient will discontinue TKI therapy one month after randomization. From then on patient will receive no further treatment.	Other: Surveillance For patients randomized into this treatment arm stopp their standard treatment and will just be under observation.

Detailed Description:

Four hypotheses are tested in hierarchical order. To avoid inflation of type 1 error (false rejection of a null hypothesis), further confirmatory testing has to be stopped as soon as a null hypothesis could not be rejected.

All four hypotheses are tested at significance level 0.05. Null hypotheses 1, 2, and 4 deal with probabilities of molecular relapse-free survival 7, 13, and 25 months after randomisation, respectively; arms A and B are compared with the uncorrected chi-square test. Null hypothesis 3 investigates molecular relapse-free survival as a time-to-event variable; the two arms are compared with the log-rank test

Eligibility

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 and older (Adult, Senior)
Sexes Eligible for Study:	All
Accepts Healthy Volunteers:	No

Criteria

Inclusion Criteria:

1. Signed written informed consent form
2. Capability and willingness to comply with study procedures and ability to self-administration of the study drug
3. Male or female aged ≥ 18 years
4. At least three years of TKI therapy
5. BCR-ABL-positive, chronic phase CML patients with a transcript level according to the international scale (IS) of at least MR4, or better (MR4.5, MR5). MR4 is defined as (i) detectable disease ≤0.01% BCR-ABL IS or (ii) undetectable disease in cDNA with ≥10,000 ABL or ≥24,000 GUS transcripts for at least one year. There have to be at least three documented PCR-results with MR4 or better within the last year (+/-2 months) before study entry. One of these PCR´s must be a confirmatory MR4 measurement prior to randomization by an EUTOS-certified laboratory at the Universities of Mannheim or Jena. No PCR-results in the last year before randomisation can be worse than MR4
6. Patients who had failed to discontinue TKI in a prior discontinuation attempt are eligible for this protocol, if they fulfil criterion 5 after retreatment with TKI. A prior TKI discontinuation failure must be specifically indicated at inclusion and documented
7. Adequate organ function:

   especially total bilirubin, lactate dehydrogenase [LDH], aspartate aminotransferase [AST], alanine aminotransferase [ALT] and coagulation parameters ≤ 2 × upper limit of normal (ULN)
8. Adequate hematological parameters:

absolute neutrophil count ≥ 1.2 × 109/L; platelet count ≥ 100 × 109/L; leukocyte count ≥ 2.5 × 109/L; lymphocytes ≥ 1.0 × 109/L; hemoglobin ≥ 9.0 g/dL or 5.59 mmol/L

9. Female patients with reproductive potential must agree to maintain highly effective methods of contraception by practicing abstinence or by using at least two methods of birth control from the date of consent through the end of the study. If abstinence could not be practiced, a combination of hormonal contraceptive (oral, injectable, or implants) and a barrier method (condom, diaphragm with a vaginal spermicidal agent) has to be used. Also male patients must agree to use condoms during study participation.
10. Negative serum pregnancy test in women of childbearing potential. Urine pregnancy test would also be accepted
11. Date of diagnosis must be known
12. The following parameters from diagnosis must be known:

    palpable spleen size enlargement in cm below costal margin, platelet count, percentages of blasts, basophils, and eosinophils in peripheral blood. These values must have been recorded. The values of the Sokal, the EURO, the EUTOS, and the ELTS score would be desirable
13. Tested HIV sero-negativity and tested negative against hepatitis B or C

Exclusion Criteria:

1. History of autoimmune disease
2. Immunosuppressive treatment of any kind
3. Prior allogeneic stem cell Transplantation
4. Prior pegylated IFN therapy. Prior low dose conventional IFN treatment with ≤ 3 x 3 Mio I.E. / week for less than 1 year is acceptable
5. Prior history of TKI resistance, accelerated phase or blast crisis
6. Hypersensitivity/allergy to the active substance or excipients of the formulation
7. Severe hepatic dysfunction or decompensated cirrhosis
8. Intake of Telbivudin
9. Thyroid disease that cannot be controlled by conventional therapy
10. Epilepsy or other disorders of the central nervous system
11. Severe cardiac disease history including unstable or uncontrolled cardiac disease in the previous 6 months
12. Any history of retinopathy e.g. retinal detachment, degeneration or thromboembolic events
13. Clinically significant concomitant diseases or conditions, which, in the opinion of the investigator, would lead to an unacceptable risk for the patient to participate in the study (please refer also to the actual Investigator Brochure)

14. Other malignancy, except adequately treated superficial bladder cancer, basal or squamous cell carcinoma of the skin, or other cancer(s) for which the patient has been disease free for more than 3 years
15. Active or uncontrolled infections at the time of randomization
16. Pregnant and/or nursing women
17. Use of antibiotic therapy within the last 2 weeks prior to randomization
18. Concurrent use of molecular targeted therapy
19. Known HIV sero-positivity or known active hepatitis B or C infection
20. Participation in another clinical study with other investigational drugs within 14 days prior to randomization
21. Vaccination within 1 month prior to randomization
22. Any medical, mental, psychological or psychiatric condition (particularly severe depression, suicidal ideation or suicide attempt) that in the opinion of the investigator would not permit the patient to complete the study or comply to study procedures
23. Drug and/or alcohol abuse

Contacts and Locations

Information from the National Library of Medicine NIH NLM

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): ***NCT03117816***

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More Information

Publications:

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Leukemia	Interferons
Leukemia, Myeloid	Interferon-alpha
Leukemia, Myelogenous, Chronic, BCR-ABL Positive	Antineoplastic Agents
	Antiviral Agents
Neoplasms by Histologic Type	Anti-Infective Agents
Neoplasms	Immunologic Factors
Myeloproliferative Disorders	Physiological Effects of Drugs

Bone Marrow Diseases
Hematologic Diseases