A Study of Imatinib Versus Nilotinib in Adult Patients With Newly Diagnosed Philadelphia Chromosome Positive (Ph+) Chronic Myelogenous Leukemia in Chronic Phase (CML-CP) (ENESTnd)

This study is ongoing, but not recruiting participants.

Sponsor:
Novartis Pharmaceuticals

Information provided by (Responsible Party):
Novartis (Novartis Pharmaceuticals)

ClinicalTrials.gov Identifier:
NCT00471497

First received: May 7, 2007
Last updated: November 19, 2014
Last verified: November 2014
History of Changes

Purpose

In this study, the efficacy and safety of tw o nilotinib doses, 300 mg tw ice daily and 400 mg tw ice daily, w ill be compared w ith imatinib 400 mg once daily in new ly diagnosed patients w ith Philadelphia chromosome-positive (Ph+) Chronic Myelogenous Leukemia in the chronic phase (CML-CP).

Condition	Intervention	Phase
Myelogenous Leukemia, Chronic	Drug: nilotinib Drug: imatinib	Phase 3

Study Type: Interventional
Study Design: Allocation: Randomized
Endpoint Classification: Safety/Efficacy Study
Intervention Model: Parallel Assignment
Masking: Open Label
Primary Purpose: Treatment

Official Title: A Phase III Multi-center, Open-label, Randomized Study of Imatinib Versus Nilotinib in Adult Patients With New ly Diagnosed Philadelphia Chromosome Positive (Ph+) Chronic Myelogenous Leukemia in Chronic Phase (CML-CP)

Resource links provided by NLM:

Genetics Home Reference related topics: tetrasomy 18p

MedlinePlus related topics: Chronic Myeloid Leukemia Leukemia

Drug Information available for: Imatinib Imatinib mesylate Nilotinib

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

U.S. FDA Resources

Further study details as provided by Novartis:

Primary Outcome Measures:

- Molecular Response Rate (MMR) at 12 Months [Time Frame: Baseline, 12 months] [Designated as safety issue: No]

  Rate of MMR is defined as <= 0.1% BCR-ABL/ABL ratio by international scale (IS), measured by real-time quantitative polymerase chain

reaction (RQ-PCR) w hich corresponds to a ≥ 3 log reduction of BCR-ABL transcript from standardized baseline. BCR-ABL = fusion gene from BCR (breakpoint cluster region gene/BCR gene product) and ABL (Abelson protooncogene)

Secondary Outcome Measures:

- Rate of Durable MMR at 24 Months. [Time Frame: Baseline, 24 months] [Designated as safety issue: No]
- Rate Reduction in BCR-ABL Transcript Levels in Nilotinib Treatment Arms With Imatinib at 12 Months [Time Frame: Baseline, 12 months] [Designated as safety issue: No]
- Rate of Complete Cytogenetic Response (CCyR) in Nilotinib Treatment Arms With Imatinib at 12 Months [Time Frame: Baseline, 12 months] [Designated as safety issue: No]

Enrollment:	846
Study Start Date:	July 2007
Estimated Study Completion Date:	October 2018
Estimated Primary Completion Date:	October 2018 (Final data collection date for primary outcome measure)

Arms	Assigned Interv entions
Experimental: nilotinib 300mg bid (investigating arm)	Drug: nilotinib Nilotinib w as supplied as 50 mg, 150 mg and 200 mg hard gelatin capsules and administered orally at 300 mg BID (tw ice a day) or 400 mg BID (tw ice a day)depending on the randomized dose. Other Name: AMN107
Experimental: Nilotinb 400 mg bid (investigating arm)	Drug: nilotinib Nilotinib w as supplied as 50 mg, 150 mg and 200 mg hard gelatin capsules and administered orally at 300 mg BID (tw ice a day) or 400 mg BID (tw ice a day)depending on the randomized dose. Other Name: AMN107
Experimental: imatinib 400mg QD (control arm)	Drug: imatinib Imatinib w as supplied as 100 mg and 400 mg tablets and administered orally at 400 mg QD (once a day). Other Name: STI571

Eligibility

Ages Eligible for Study:	18 Years and older
Genders Eligible for Study:	Both
Accepts Healthy Volunteers:	No

Criteria

Inclusion criteria:

- Chronic myelogenous leukemia in chronic phase patients w ithin the first 6 months of diagnosis.
- Diagnosis of chronic myelogenous leukemia in chronic phase w ith confirmation of Philadelphia chromosome

Exclusion criteria:

- Treatment w ith a tyrosine kinase inhibitor prior to study entry is not allow ed except for no more than 2 w eeks in duration of imatinib
- Any medical treatment for CML prior to study entry for longer than 2 w eeks w ith the exception of hydroxyurea and/or anagrelide
- Uncontrolled or significant cardiovascular disease.
- Severe or uncontrolled medical conditions (i.e. uncontrolled diabetes, active or uncontrolled infection).
- Use of therapeutic coumarin derivatives (i.e., w arfarin, acenocoumarol, phenprocoumon)
- Currently taking certain medications that could affect the rhythm of your heart.

Other protocol-defined inclusion/exclusion criteria may apply

Contacts and Locations

Choosing to participate in a study is an important personal decision. Talk w ith 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, see Learn About Clinical Studies.

Please refer to this study by its ClinicalTrials.gov identifier: NCT00471497

Show 220 Study Locations

Sponsors and Collaborators

Novartis Pharmaceuticals

Investigators

Study Director: Novartis Pharmaceuticals Novartis Pharmaceuticals

More Information

Additional Information:

Visit NovartisClinicalTrials.com: Pre-qualify for a trial, and view a list of trials and participating study centers.

No publications provided by Novartis

Additional publications automatically indexed to this study by ClinicalTrials.gov Identifier (NCT Number):

Hughes TP, Hochhaus A, Kantarjian HM, Cervantes F, Guilhot F, Niederwieser D, le Coutre PD, Rosti G, Ossenkoppele G, Lobo C, Shibayama H, Fan X, Menssen HD, Kemp C, Larson RA, Saglio G. Safety and efficacy of switching to nilotinib 400 mg twice daily for patients with chronic myeloid leukemia in chronic phase with suboptimal response or failure on front-line imatinib or nilotinib 300 mg twice daily. Haematologica. 2014 Jul;99(7):1204-11. doi: 10.3324/haematol.2013.091272. Epub 2014 Feb 14.

Hughes TP, Saglio G, Kantarjian HM, Guilhot F, Niederwieser D, Rosti G, Nakaseko C, De Souza CA, Kalaycio ME, Meier S, Fan X, Menssen HD, Larson RA, Hochhaus A. Early molecular response predicts outcomes in patients with chronic myeloid leukemia in chronic phase treated with frontline nilotinib or imatinib. Blood. 2014 Feb 27;123(9):1353-60. doi: 10.1182/blood-2013-06-510396. Epub 2013 Dec 11.

Hochhaus A, Saglio G, Larson RA, Kim DW, Etienne G, Rosti G, De Souza C, Kurokawa M, Kalaycio ME, Hoenekopp A, Fan X, Shou Y, Kantarjian HM, Hughes TP. Nilotinib is associated with a reduced incidence of BCR-ABL mutations vs imatinib in patients with newly diagnosed chronic myeloid leukemia in chronic phase. Blood. 2013 May 2;121(18):3703-8. doi: 10.1182/blood-2012-04-423418. Epub 2013 Mar 15.

Branford S, Kim DW, Soverini S, Haque A, Shou Y, Woodman RC, Kantarjian HM, Martinelli G, Radich JP, Saglio G, Hochhaus A, Hughes TP, Müller MC. Initial molecular response at 3 months may predict both response and event-free survival at 24 months in imatinib-resistant or -intolerant patients with Philadelphia chromosome-positive chronic myeloid leukemia in chronic phase treated with nilotinib. J Clin Oncol. 2012 Dec 10;30(35):4323-9. doi: 10.1200/JCO.2011.40.5217. Epub 2012 Oct 29.

Larson RA, Yin OQ, Hochhaus A, Saglio G, Clark RE, Nakamae H, Gallagher NJ, Demirhan E, Hughes TP, Kantarjian HM, le Coutre PD. Population pharmacokinetic and exposure-response analysis of nilotinib in patients with newly diagnosed Ph+ chronic myeloid leukemia in chronic phase. Eur J Clin Pharmacol. 2012 May;68(5):723-33. doi: 10.1007/s00228-011-1200-7. Epub 2011 Dec 30.

Kantarjian HM, Hochhaus A, Saglio G, De Souza C, Flinn IW, Stenke L, Goh YT, Rosti G, Nakamae H, Gallagher NJ, Hoenekopp A, Blakesley RE, Larson RA, Hughes TP. Nilotinib versus imatinib for the treatment of patients with newly diagnosed chronic phase, Philadelphia chromosome-positive, chronic myeloid leukaemia: 24-month minimum follow-up of the phase 3 randomised ENESTnd trial. Lancet Oncol. 2011 Sep;12(9):841-51. doi: 10.1016/S1470-2045(11)70201-7. Epub 2011 Aug 17. Erratum in: Lancet Oncol. 2011 Oct;12(11):989.

Cortes JE, Hochhaus A, le Coutre PD, Rosti G, Pinilla-Ibarz J, Jabbour E, Gillis K, Woodman RC, Blakesley RE, Giles FJ, Kantarjian HM, Baccarani M. Minimal cross-intolerance with nilotinib in patients with chronic myeloid leukemia in chronic or accelerated phase who are intolerant to imatinib. Blood. 2011 May 26;117(21):5600-6. doi: 10.1182/blood-2010-11-318949. Epub 2011 Apr 5.

Saglio G, Kim DW, Issaragrisil S, le Coutre P, Etienne G, Lobo C, Pasquini R, Clark RE, Hochhaus A, Hughes TP, Gallagher N, Hoenekopp A, Dong M, Haque A, Larson RA, Kantarjian HM; ENESTnd Investigators. Nilotinib versus imatinib for newly diagnosed chronic myeloid leukemia. N Engl J Med. 2010 Jun 17;362(24):2251-9. doi: 10.1056/NEJMoa0912614. Epub 2010 Jun 5.

Responsible Party:	Novartis (Novartis Pharmaceuticals)
ClinicalTrials.gov Identifier:	NCT00471497 History of Changes
Other Study ID Numbers:	**CAMN107A2303**, 2007-000208-34
Study First Received:	May 7, 2007
Results First Received:	April 10, 2013
Last Updated:	November 19, 2014
Health Authority:	United States: Food and Drug Administration Argentina: Administracion Nacional de Medicamentos, Alimentos y Tecnologia Medica Austria: Ethikkommission Belgium: Federal Agency for Medicinal Products and Health Products Brazil: Ministry of Health Canada: Health Canada Colombia: INVIMA Instituto Nacional de Vigilancia de Medicamentos y Alimentos

Czech Republic: State Institute for Drug Control
Denmark: Danish Medicines Agency
Egypt: Ministry of Health and Population
Finland: Finnish Medicines Agency
France: Afssaps - Agence française de sécurité sanitaire des produits de santé (Saint-Denis)
Germany: Federal Institute for Drugs and Medical Devices
Hong Kong: Department of Health
Hungary: Research Ethics Medical Committee
Italy: Ministry of Health
Japan: Pharmaceuticals and Medical Devices Agency
Korea: Food and Drug Administration
Malaysia: Ministry of Health
Mexico: Ministry of Health
Netherlands: Medicines Evaluation Board (MEB)
Norway: Norwegian Medicines Agency
Poland: Ministry of Health
Russia: Ministry of Health of the Russian Federation
Singapore: Clinical Trials & Epidemiology Research Unit (CTERU)
Slovakia: State Institute for Drug Control
South Korea: Korea Food and Drug Administration (KFDA)
Spain: Agencia Española de Medicamentos y Productos Sanitarios
Sweden: Medical Products Agency
Switzerland: Swissmedic
Taiwan: Department of Health
Thailand: Food and Drug Administration
Turkey: Ministry of Health
United Kingdom: Medicines and Healthcare Products Regulatory Agency
Venezuela: Ministry of Health and Social Development

Keywords provided by Novartis:
leukemia
bone marrow
leukemia symptoms
lukemia
cml
complete blood count
lymphocyte
blood cancer
leukocytes
chronic leukemia
bone marrow biopsy
leukemia research
leukemia cells
bone marrow disease
chronic myeloid leukemia
blood cancer symptoms
white blood cell diseases
chronic myelogenous leukemia
leukemia treatment
leukemia facts
leucemia
facts about leukemia
myelogenous leukemia
newly diagnosed CML
newly diagnosed Philadelphia chromosome positive (Ph+) chronic myelogenous leukemia in chronic phase (CML-CP)

Additional relevant MeSH terms:
Abnormal Karyotype
Leukemia
Leukemia, Myelogenous, Chronic, BCR-ABL Positive
Leukemia, Myeloid
Philadelphia Chromosome
Bone Marrow Diseases
Chromosome Aberrations
Hematologic Diseases
Myeloproliferative Disorders
Neoplasms
Neoplasms by Histologic Type
Pathologic Processes
Translocation, Genetic
Imatinib
Antineoplastic Agents
Enzyme Inhibitors
Molecular Mechanisms of Pharmacological Action
Pharmacologic Actions
Protein Kinase Inhibitors
Therapeutic Uses

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