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Completed ⓘ

Study of Macitentan (ACT-064992) on Morbidity and Mortality in Patients With Symptomatic Pulmonary Arterial Hypertension (SERAPHIN)

ClinicalTrials.gov ID ⓘ NCT00660179

Sponsor ⓘ Actelion

Information provided by ⓘ Actelion (Responsible Party)

Last Update Posted ⓘ 2015-09-28

Study Details Tab

Study Overview

Brief Summary

The AC-055-302/SERAPHIN study will be an event-driven Phase III study, comparing two different doses of macitentan (ACT-064992) (3 and 10 mg) vs placebo in patients with symptomatic PAH. The main study objective is to demonstrate that macitentan (ACT-064992) prolongs time to the first morbidity or mortality event, and to evaluate the benefit/risk profile of macitentan (ACT-064992) in the treatment of patients with symptomatic PAH.

Official Title

A Multicenter, Double-blind, Randomized, Placebo-controlled, Parallel Group, Event-driven, Phase III Study to Assess the Effects of Macitentan (ACT-064992) on Morbidity and Mortality in Patients With Symptomatic Pulmonary Arterial Hypertension

Conditions ⓘ

Pulmonary Arterial Hypertension

Intervention / Treatment ⓘ

- Drug: macitentan (ACT-064992)
- Drug: macitentan (ACT-064992)
- Drug: placebo

Other Study ID Numbers ⓘ

Study Start ⓘ
2008-05
Primary Completion (Actual) ⓘ
2012-03
Study Completion (Actual) ⓘ
2012-04
Enrollment (Actual) ⓘ
742
Study Type ⓘ
Interventional
Phase ⓘ
Phase 3

Resource links provided by the National Library of Medicine

[MedlinePlus Genetics](https://medlineplus.gov/genetics/) (<https://medlineplus.gov/genetics/>), related topics: [Pulmonary arterial hypertension](https://medlineplus.gov/genetics/condition/pulmonary-arterial-hypertension) (<https://medlineplus.gov/genetics/condition/pulmonary-arterial-hypertension>), [Hypertension](https://medlineplus.gov/genetics/condition/hypertension) (<https://medlineplus.gov/genetics/condition/hypertension>).

[MedlinePlus](https://medlineplus.gov/) (<https://medlineplus.gov/>), related topics: [Drug Safety](https://medlineplus.gov/drugsafety.html) (<https://medlineplus.gov/drugsafety.html>).

[Genetic and Rare Diseases Information Center](https://rarediseases.info.nih.gov/gard) (<https://rarediseases.info.nih.gov/gard>), resources: [Pulmonary arterial hypertension](https://rarediseases.info.nih.gov/?gard_id=0007501) (https://rarediseases.info.nih.gov/?gard_id=0007501).

[Drug Information](https://dailymed.nlm.nih.gov/dailymed/) (<https://dailymed.nlm.nih.gov/dailymed/>), available for: [Macitentan](https://dailymed.nlm.nih.gov/dailymed/search.cfm?labeltype=human&query=Macitentan) (<https://dailymed.nlm.nih.gov/dailymed/search.cfm?labeltype=human&query=Macitentan>).

[FDA Drug and Device Resources](https://clinicaltrials.gov/fda-links) (<https://clinicaltrials.gov/fda-links>).

Contacts and Locations

This section provides contact details for people who can answer questions about joining this study, and information on where this study is taking place.

To learn more, please see the [Contacts and Locations section in How to Read a Study Record](https://clinicaltrials.gov/study-basics/how-to-read-study-record#contacts-and-locations) (<https://clinicaltrials.gov/study-basics/how-to-read-study-record#contacts-and-locations>).

This study has 153 locations

United States

Alabama Locations

-  **Birmingham, Alabama, United States, 35249-0001**
University of Alabama at Birmingham

Arizona Locations

-  **Phoenix, Arizona, United States, 85013**
Arizona Pulmonary Specialists

California Locations

-  **Los Angeles, California, United States**
GLVA Healthcare Center
-  **San Diego, California, United States**
University of California, San Diego
-  **Santa Barbara, California, United States**
Santa Barbara Cottage Hospital
-  **Torrance, California, United States**
Liu Center for Pulmonary Hypertension

Colorado Locations

-  **Denver, Colorado, United States**
University of Colorado Health Sciences Center

Florida Locations

-  **Jacksonville, Florida, United States**
Mayo Clinic, Jacksonville

Georgia Locations

-  **Atlanta, Georgia, United States, 30322**
Emory University Hospital - McKelvey Center for Lung Transplantation & Pulmonary Vascular Disease
-  **Atlanta, Georgia, United States, 30342**
Pulmonary & Critical Care of Atlanta
-  **Decatur, Georgia, United States**
Southeastern Lung Care

Illinois Locations

-  **Chicago, Illinois, United States**
University of Chicago Hospitals

Iowa Locations

-  **Iowa City, Iowa, United States**
University of Iowa

Kansas Locations

-  **Kansas City, Kansas, United States, 66160**
University of Kansas Medical Center

Kentucky Locations

-  **Louisville, Kentucky, United States**
Kentuckiana Pulmonary Associate, PLLC

Louisiana Locations

-  **New Orleans, Louisiana, United States**
Medical Center of Louisiana at New Orleans

Maine Locations

-  **Portland, Maine, United States, 04102**
Maine Medical Center

Maryland Locations

-  **Baltimore, Maryland, United States, 21201**
University of Maryland School of Medicine

Massachusetts Locations

-  **Boston, Massachusetts, United States**
Boston University School of Medicine
-  **Boston, Massachusetts, United States**
Pulmonary/Critical Care Division/Tufts New England Medical Center

Michigan Locations

-  **Ann Arbor, Michigan, United States**
University of Michigan

Missouri Locations

-  **St Louis, Missouri, United States, 63110**
Washington University School of Medicine

New Jersey Locations

-  **New Brunswick, New Jersey, United States**
University of NJ - Robert Wood Johnson Medical School

New York Locations

-  **New York, New York, United States**
Columbia University Medical Center - Pediatric Cardiology

North Carolina Locations

-  **Durham, North Carolina, United States**
Duke University Medical Center

Ohio Locations

-  **Cincinnati, Ohio, United States**
University of Cincinnati Ohio Heart Health Center
-  **Columbus, Ohio, United States, 43210**
Ohio State University

Tennessee Locations

-  **Nashville, Tennessee, United States**
Vanderbilt University Medical Center

Texas Locations

-  **Dallas, Texas, United States, 75235**
University of Texas Medical Center - St. Paul University
-  **Houston, Texas, United States, 77030**
Baylor College of Medicine and the Methodist Hospital

Utah Locations

-  **Salt Lake City, Utah, United States**
Dept. of Pulmonary Medicine - Latter Day Saints Hospital

Virginia Locations

-  **Norfolk, Virginia, United States, 23507**
Sentara Hospital T/A Sentara Cardiovascular Research Institute

Wisconsin Locations

-  **Milwaukee, Wisconsin, United States**
Comprehensive Cardiovascular Care Group

Argentina

-  **Buenos Aires, Argentina, C1093AAS**
Fundacion Favaloro
-  **Buenos Aires, Argentina**

Hospital Britanico

 Buenos Aires, Argentina

Sanatorio MITRE

 Buenos Aires, Argentina

SANATORIO OTAMENDI y MIROLI

 Corrientes, Argentina

Instituto Cardiologia Corrientes

 Córdoba, Argentina

Htal Italiano Cordoba

 Córdoba, Argentina

Htla privado de Cordoba

 Santa Fe, Argentina

'Hospital Italiano - Garibaldi de Rosario

Australia

 Darlinghurst, NSW, Australia, 2010

St. Vincent's Hospital

 Melbourne, VIC, Australia, 3181

The Alfred Hospital

 Sunshine Coast, Australia, 4558

Royal Brisbane Hospital

Austria

 Vienna, AustriaMedical University of Vienna/ Department of Internal Medicine II,
Division of Cardiology**Belarus**

 Minsk, Belarus, 220036

Republican reserach - Pratical Centre of Cardiology

 Minsk, Belarus, 223040

Minsk Regional Clinical Hospital

 Vitebsk, Belarus, 210037

Vitebsk Regional Clinical Hospital

Belgium

 Leuven, BelgiumUniversity Hospital Gasthuisberg / Kliniekhoofd, Interne Geneeskunde -
I.G. Pneumologie**Bulgaria**

 Sofia, Bulgaria, 1309Specialized Hospital for Active Treatment of Cardio-Vascular Diseases
/ Department of Pediatric Cardiology**Canada**

 Calgary, Canada

Peter Lougheed Centre

 Toronto, Canada

Toronto General Hospital

 Vancouver, Canada, V6Z 1Y6

Vancouver General Hospital

Ontario Locations **London, Ontario, Canada**

London Health Sciences Centre / Victoria Hospital

Quebec Locations

-  **Saint-Foy, Quebec, Canada**
L'Hopital Laval

Chile

Chile Locations

-  **Santiago, Chile, Chile**
'Pontificia Universidad Catolica de Chile
-  **Santiago, Chile, Chile**
Hospital del Torax
-  **Santiago, Chile, Chile**
Hospital San Juan de Dios

China

-  **Beijing, China, 100029**
Beijing Anzhen Hospital of the Capital University of Medical Sciences, Cardiology Department
-  **Beijing, China, 100032**
Peking Union Medcical College Hospital, Rheumatology Department
-  **Beijing, China, 100853**
Chinese PLA General Hospital (301 Hospital), Cardiology Department
-  **Shanghai, China, 200001**
Renji Hospital, Rheumatology Dept
-  **Shanghai, China, 200032**
Zhongshan Hospital Fudan University, Cardiology Dept
-  **Shanghai, China, 200127**
Renji Hospital, Cardiology Dept
-  **Shanghai, China, 200433**
Shanghai Pulmonary Hospital, Dept of Pulmonary Circulation

Guangdong Locations

-  **Guangzhou, Guangdong, China, 510080**
Guangdong General Hospital, Cardiology Department

Jiangsu Locations

-  **Nanjing, Jiangsu, China, 210029**
Jiangsu Province Hospital - Pneumology Department

Colombia

-  **Bogotá, Colombia**
Fundación Clínica Shaio
-  **Floridablanca, Santander, Colombia**
'Fundacion Cardiovascular de Colombia

Croatia

-  **Rijeka, Croatia, 51 000**
Clinical Hospital Center

France

-  **Clamart, France, 92140**
Hôpital Antoine Bécclère / Service de Pneumologie
-  **Montpellier, France, 34295**
Hôpital Arnaud de Villeneuve Service des Maladies Respiratoires
-  **Pessac, France, 33604**
Hopital Haut-Leveque - Maison du Haut-Leveque

Germany

-  **Berlin, Germany**
Unfallkrankenhaus Berlin, Klinik für Innere Medizin
-  **Cologne, Germany, D-50924**
Universität zu Köln, Medizinische Klinik III, Abteilung Kardiologie
-  **Dresden, Germany, D-01307**
Medizinische Klinik und Poliklinik I Universitätsklinikum Carl Gustav Carus
-  **Giessen, Germany, D-35392**
Universitätsklinikums Gießen und Marburg GmbH / Medizinische Klinik und Poliklinik II, Innere Med.
-  **Greifswald, Germany, D-17487**
Universität Greifswald / Klinik für Innere Medizin B,
-  **Hamburg, Germany, D-20246**
Universitätsklinikum Hamburg-Eppendorf / Onkologie, Hämatologie und Knochenmarktransplantation mit Sektion Pneumologie
-  **Heidelberg, Germany, D-69126**
Thoraxklinik am Universitätsklinikum Heidelberg
-  **Homburg/Saar, Germany, D-66421**
Universitätskliniken des Saarlandes / Medizinische Klinik und Poliklinik, Innere Medizin V
-  **Leipzig, Germany, 04103**
Universitätsklinik Leipzig
-  **Mainz, Germany, D-55131**
Klinikum der Johannes Gutenberg-Universität / II. Medizinische Klinik und Poliklinik
-  **Munich, Germany, D-81377**
Medizinische Klinik und Poliklinik I der Ludwig-Maximilians-Universität München / Klinikum Großhadern, Schwerpunkt Pneumologie
-  **Regensburg, Germany, 93053**
Universitätsklinikum Regensburg / Innere Medizin II

Hong Kong

-  **Hong Kong, Hong Kong**
Prince of Wales Hospital/ Division of Rheumatology, Department of Medicine & Therapeutics
-  **Hong Kong, Hong Kong**
Queen Mary Hospital / Division of Cardiology, Department of Medicine

Hungary

-  **Budapest, Hungary, H-1096**
Gottsegen György Országos Kardiológiai Intézet (Hungarian Institute of Cardiology)
-  **Budapest, Hungary, H-1125**
Semmelweis University, Pulmonology Clinic
-  **Szeged, Hungary**
University of Szeged Albert Szent-Györgyi Medical and Pharmaceutical Center, Faculty of General Medicine, II. Internal Medicine Clinic, Cardiology Center

India

-  **Ahmedabad, India, 382428**
Life Care Institute of Medical Science & Research, Ahmedabad
-  **Delhi, India, 110049**
G B Pant Hospital & Maulana Azad Medical College
-  **Hyderabad, India, 500001**

Care Hospital

 Mumbai, India, 400 012

King Edward VII Memorial Hospital (KEM) Hospital

 Mumbai, India, 400016P D Hinduja National Hospital and Medical Research Centre/
Pulmonary Medicine **Pune, India, 411 004**

Deenanath Mangeshkar Hospital and Research Centre

Israel **Haifa, Israel, 34362**Lady Davis Carmel Medical Center / Department of Cardiovascular
Medicine, Pulmonary Division **Petach - Tikvah, Israel, 49100**

Rabin Medical Center - Belinson campus - Pulmonary Institute

 Rehovot, Israel, 76100

Pulmonary Institute, Kaplan Medical Center

 Tel Aviv, Israel, 64239

Sourasky Medical Center - Division of Pulmonary Medicine and Allergy

 Tel Litwinsky, Israel, 52621

The pulmonary institute Sheba Medical centre

Italy **Roma, Italy, 00161**

Policlinico Umberto I, Cardiologia

Malaysia **Kuala Lumpur, Malaysia, 50400**

Institut Jantung Negara (National Heart Institute)

Mexico **Mexico City, Mexico, 14080**

'Instituto Nacional de Cardiología (INC) Ignacio Chávez

 Monterrey Nuevo León, Mexico, 64020

Unidad de Investigación Clínica en Medicina, SC

Netherlands **Nieuwegein, Netherlands, 3435 CM**

St. Antonius ziekenhuis

Norway **Oslo, Norway, N0514**

Aker University Dept of Cardiology

Peru **Lima, Peru**

Hospital Alberto Sabogal Sologuren - EsSALUD

 Lima, Peru

Instituto de Enfermedades Respiratorias, Clínica San Gabriel

Poland **Krakow, Poland, 31-202**Klinika Chorob Serca i Naczyn Instytut Kardiologii Collegium Medicum
UJ **Warsaw, Poland, 01-138**

Klinika Chorób Wewnętrznych Klatki Piersiowej

- Zabrze, Poland, 41-800**
III Katedra i Oddział Kliniczny Kardiologii Śląskiego Uniwersytetu Medycznego

Romania

- Bucharest, Romania, 022328**
Institutul de boli cardiovasculare / Clinica de Cardiologie
- Bucharest, Romania, 50159**
Institutul de Pneumologie "Marius Nasta" / I. Clinica de Pneumoftiziologie

Russia

- Kemerovo, Russia, 650002**
Municipal Health Care Institution "Kemerovo Cardiology Dispensary"
- Moscow, Russia, 105077**
Federal State Institution "Scientific Research Institute of Pulmonology of Roszdrav"
- Moscow, Russia, 117049**
State Health Care Institution of Moscow "City Clinical Hospital #1 named after N. I. Pirogov"
- Moscow, Russia, 121552**
Federal State Institution "Russian Cardiology Scientific and Production Complex of Rosmedtechnology"
- Saint Petersburg, Russia, 194156**
Federal State Institution "Federal Center of Heart, Blood and Endocrinology named after V.A. Almazov" of Rosmedtechnology
- Saint Petersburg, Russia, 197 022**
State Educational Institution of High Professional Education
- Tomsk, Russia, 634063**
State Institution "Scientific Research Institute of Cardiology" of Tomsk Scientific Center of RAMS, Siberian branch
- Tomsk, Russia, 634063**
Tomsk Regional Clinical Hospital / Pulmonology Unit
- Yaroslavl, Russia, 150 003**
Municipal Health Care Institution "Clinical Hospital of Emergency Care named after N.V. Soloviov"
- Yekaterinburg, Russia, 620102**
Sverdlovsk Regional Clinical Hospital # 1/ Cardiology Department (2nd Therapy Department)

Serbia

- Belgrade, Serbia, 11000**
University Children's Hospital (UNIVERZITETSKA DEČJA KLINIKA)
- Belgrade, Serbia, 11000**
University Clinical Center of Serbia / Institute for Lung Diseases and Tuberculosis
- Belgrade, Serbia, 11080**
Zemun Clinical Hospital (Kliničko-bolnički centar "Zemun") / Department of Cardiology

Singapore

- Singapore, Singapore, 168752**
National University Hospital/ The Heart Institute
- Singapore, Singapore, 168752**
Singapore General Hospital

Slovakia

- Bratislava, Slovakia, 833 48**
National Institute of Cardiovascular Diseases (Národný ústav srdcových a cievnych chorôb, a.s. - NÚSCH) / Department of Heart Transplantation
- Bratislava, Slovakia, 833 48**
Slovak Medical University (Slovenská zdravotnícka univerzita) / Faculty of Medical Speciality Studies (Fakulta zdravotníckych špecializačných štúdií), Department of Cardiology and Angiology

South Africa

- Johannesburg, South Africa, 2000**
Netcare Milpark Hospital, Center for Chest Disease
- Johannesburg, South Africa, 27-11-033 8197**
Chris Hani Baragwanath Hospital, Department of Cardiology
- Parow, South Africa, 7505**
Tread Research
- Somerset West, South Africa, 7130**
Block 4, Vergelegen Medi-Clinic

Spain

- A Coruña, Spain, 15006**
Hospital Juan Canalejo Servicio de Neumología
- Barcelona, Spain, 08035**
Hospital Universitario Vall d'Hebron, Pneumology Unit, Planta Baja
Hospital General
- Barcelona, Spain, 08036**
Hospital Clínico I Provincial, Servicio de Neumología.
- Madrid, Spain, 20841**
Hospital 12 Octubre/ Cardiology department Planta 5a.
- Málaga, Spain, 29010**
Hospital Clínico Virgen de la Victoria / Pneumology Unit,
- Pontevedra, Spain, 36771**
Hospital Montecelo, Servicio de Neumología

Sweden

- Lund, Sweden, SE-221 85**
University Hospital in Lund, Heart and Lung Division
- Uppsala, Sweden, 751 85**
Servicio de Medicina Interna, Unidad de Hipertensión Pulmonar

Taiwan

- Taichung, Taiwan, 40705**
Taichung Veterans General Hospital / Division of Allergy, Immunology and Rheumatology
- Taipei, Taiwan**
National Taiwan University Hospital/ Thoracic Surgical Division, Surgical Department

Thailand

- Bangkok, Thailand, 10400**
Ramathibodi Hospital, Mahidol University, Cardiology Unit, Department of Medicine,
- Bangkok, Thailand, 10700**
Siriraj Hospital/ Department of Pediatrics, Faculty of Medicine, Siriraj Hospital, Mahidol University
- Chiang Mai, Thailand**
Chiang Mai Hospital / Division of Rheumatology, Department of Medicine, Faculty of Medicine, Chiang Mai University

 **Khon Kaen, Thailand, 40002**
Srinagarind Hospital/Division of Rheumatology, Department of
Medicine, Faculty of Medicine, Khon Kaen University

Turkey (Türkiye)

 **Istanbul, Turkey (Türkiye)**
Istanbul University Cardiology Institute

Ukraine

 **Dnipro, Ukraine, 49060**
Dnipropetrovsk State Medical Academy / Regional Diagnostic Center,
Department of electrophysiologic researches and anaesthesiologic aid

 **Lviv, Ukraine, 79010**
Danylo Halytskyi Lviv State Medical University

United Kingdom

 **London, United Kingdom, NW3 2QG**
Royal Free Hospital

Participation Criteria

Researchers look for people who fit a certain description, called [eligibility criteria](#). Some examples of these criteria are a person's general health condition or prior treatments.

For general information about clinical research, read [Learn About Studies \(https://clinicaltrials.gov/study-basics/learn-about-studies\)](https://clinicaltrials.gov/study-basics/learn-about-studies).

Eligibility Criteria

Description

Inclusion Criteria:

1. Signed informed consent prior to initiation of any study mandated procedure.
2. Patients with symptomatic pulmonary arterial hypertension (PAH) in modified World Health Organization (WHO) functional class II to IV.
3. Patients with the following types of pulmonary arterial hypertension (PAH) belonging to groups 1.1 to 1.3 of the Venice classification:
 - Idiopathic (IPAH);
 - Familial (FPAH); or
 - Related to:
 - Collagen vascular disease;
 - Simple, congenital systemic-to-pulmonary shunts at least 1 year post surgical repair;
 - Human immunodeficiency virus (HIV) infection; or
 - Drugs and toxins.
4. PAH diagnosis confirmed by hemodynamic evaluation performed prior to randomization and showing all of the following:
 - Mean pulmonary artery pressure (mPAP) > 25 mmHg at rest;
 - Pulmonary capillary wedge pressure (PCWP) or left ventricular end diastolic pressure (LVEDP) < 15 mmHg; and
 - Pulmonary vascular resistance (PVR) at rest $\geq 320 \text{ dyn} \times \text{sec} / \text{cm}^5$.
5. 6-minute walk distance (6MWD) $\geq 50 \text{ m}$.
6. Men or women > 12 years of age (women of childbearing potential must have a negative pre-treatment serum pregnancy test and must use a reliable method of contraception).

Exclusion Criteria:

1. PAH associated with portal hypertension, thyroid disorders, glycogen storage disease, Gaucher's disease, hereditary hemorrhagic telangiectasia, hemoglobinopathies, myeloproliferative disorders or splenectomy.
2. PAH associated with non corrected simple congenital systemic-to-pulmonary shunts, and combined and complex systemic-to-pulmonary shunts, corrected or non corrected.
3. PAH associated with significant venous or capillary involvement (PCWP > 15 mmHg), known pulmonary veno-occlusive disease, and pulmonary capillary hemangiomatosis.
4. Persistent pulmonary hypertension of the newborn.
5. Pulmonary Hypertension belonging to groups 2 to 5 of the Venice classification.
6. Moderate to severe obstructive lung disease: forced expiratory volume in 1 second/forced vital capacity (FEV1/FVC) < 70% and FEV1 < 65% of predicted value after bronchodilator administration.
7. Moderate to severe restrictive lung disease: total lung capacity (TLC) < 60% of predicted value.
8. Moderate to severe hepatic impairment, i.e., Child-Pugh Class B or C.
9. Estimated creatinine clearance < 30 mL/min
10. Serum aspartate aminotransferase (AST) and/or alanine aminotransferase (ALT) > 1.5 times the upper limit of normal.
11. Hemoglobin < 75% of the lower limit of the normal range.
12. Systolic blood pressure < 100 mmHg.
13. Acute or chronic physical impairment (other than dyspnea), limiting the ability to comply with study requirements.
14. Pregnant or breast-feeding.
15. Known concomitant life-threatening disease with a life expectancy < 12 months.
16. Body weight < 40 kg.
17. Any condition that prevents compliance with the protocol or adherence to therapy.
18. Recently started (< 8 weeks prior to randomization) or planned cardio-pulmonary rehabilitation program based on exercise.
19. Treatment with endothelin receptor antagonists (ERAs) within 3 months prior to randomization.
20. Systemic treatment within 4 week prior to randomization with cyclosporine A or tacrolimus, everolimus, sirolimus (calcineurin or mammalian target of rapamycin (mTOR) inhibitors).
21. Treatment with cytochrome P3A (CYP3A) inducers within 4 weeks prior to randomization
22. Known hypersensitivity to drugs of the same class as the study drug, or any of their excipients.

23. Planned treatment, or treatment, with another investigational drug within 1 month prior to randomization.

Ages Eligible for Study ⓘ

12 Years and older (Child, Adult, Older Adult)

Sexes Eligible for Study ⓘ

All

Accepts Healthy Volunteers ⓘ

No

Study Plan

This section provides details of the study plan, including how the study is designed and what the study is measuring.

How is the study designed?

Design Details

Primary Purpose ⓘ : Treatment

Allocation ⓘ : Randomized

Interventional Model ⓘ : Parallel Assignment

Masking ⓘ : Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor)

Arms and Interventions

Participant Group/Arm ⓘ	Intervention/Treatment ⓘ
Experimental: 1 Macitentan (ACT-064992) tablet, 3 mg, once daily	Drug: macitentan (ACT-064992) • Tablet, 3 mg dosage, once daily
Experimental: 2 Macitentan (ACT-064992) tablet, 10 mg, once daily	Drug: macitentan (ACT-064992) • Tablet, 10 mg dosage, once daily
Placebo Comparator: 3 Matching placebo, once daily	Drug: placebo • Matching placebo, once daily

What is the study measuring?

Primary Outcome Measures ⓘ

Outcome Measure	Measure Description	Time Frame
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Time to First Confirmed Morbidity or Mortality Event up to the End of Treatment (Kaplan-Meier Estimate of Patients Without a Morbidity or Mortality Event)	<p>Morbidity or mortality events were defined as: a) Death; b) Atrial septostomy; c) Lung transplantation; d) Initiation of intravenous (i.v.) or subcutaneous prostanoids, or; e) Other worsening of pulmonary arterial hypertension (PAH).</p> <p>Other worsening of PAH was defined by the combined occurrence of all the following 3 events:</p> <p>At least 15% decrease in the 6 minute walk distance from baseline, confirmed by 2 tests performed on separate days, within 2 weeks.</p> <p>AND worsening of PAH symptoms including at least one of the following:</p> <p>a) Increase in WHO Functional Class (WHO FC), or no change in patients in WHO FC IV at baseline; b) Appearance or worsening of signs of right heart failure that did not respond to optimized oral diuretic therapy</p> <p>AND need for new treatment(s) for PAH that included the following:</p> <p>a) Oral or inhaled prostanoids; b) Oral phosphodiesterase inhibitors; c) Endothelin receptor antagonists (only after discontinuation of study treatment; d) i.v. diuretics</p>	Up to end of treatment (data presented up to month 36)
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Secondary Outcome Measures ⓘ

Outcome Measure	Measure Description	Time Frame
Time to Death Due to PAH or Hospitalisation for PAH up to the End of Treatment (Kaplan-Meier Estimate of Patients Without an Event)	Events of PAH or hospitalization for PAH up to the end of treatment included: death due to PAH, or onset of a treatment-emergent adverse event with a fatal outcome due to PAH occurring up to 4 weeks after the end of treatment, or hospitalisation for PAH up to the end of treatment.	Up to end of treatment (data presented up to month 36)
Time to Death Due to Any Cause up to the End of Treatment (Kaplan-Meier Estimate of Patients Without an Event)	Events of death due to any cause up to the end of treatment (plus 7 days)	Up to end of treatment (data presented up to month 36)
Time to Death Due to Any Cause up to the End of Study (Kaplan-Meier Estimate of Patients Without an Event)	Events of death due to any cause up to the end of study (EOS). The initiation of EOS procedure occurred when the target of 285 events was expected to have been achieved (30 January 2012).	Up to end of study (data presented up to month 36)

Change From Baseline to Month 6 in 6-minute Walk Distance	The 6-minute walk test (6MWT) is a non-encouraged test, performed in a 30 m long flat corridor, where the patient is instructed to walk as far as possible, back and forth around two cones, with the permission to slow down, rest, or stop if needed. These guidelines were provided to all sites. For patients who had never performed a 6MWT previously, a training test was required before the qualifying tests for inclusion were performed.	Baseline to month 6
Number of Patients With Improvements in World Health Organization Functional Class From Baseline to Month 6	<p>Class I: no limitation of usual physical activity (PA) which does not increase dyspnea, fatigue, chest pain, or presyncope.</p> <p>Class II: mild limitation of PA. No discomfort at rest. Normal PA increases dyspnea, fatigue, chest pain, or presyncope.</p> <p>Class III: marked limitation of PA. No discomfort at rest. Less than ordinary activity increases dyspnea, fatigue, chest pain, or presyncope.</p> <p>Class IV: unable to perform any PA and who may have signs of right ventricular failure. Dyspnea and/or fatigue may be present at rest and symptoms are increased by almost any PA.</p>	Baseline to month 6
Pulmonary Vascular Resistance at Baseline and Month 6	In a sub-study, hemodynamic variables were assessed at baseline and Month 6. If the patient had undergone a right heart catheterization during the 3 months prior to randomization, these results were to be used as baseline values, if the background therapy had not changed during the intervening period.	Baseline to month 6
Cardiac Index at Baseline and Month 6	In a sub-study, hemodynamic variables were assessed at baseline and Month 6. If the patient had undergone a right heart catheterization during the 3 months prior to randomization, these results were to be used as baseline values, if the background therapy had not changed during the intervening period.	Baseline to month 6

Other Outcome Measures ⓘ

Outcome Measure	Measure Description	Time Frame
Summary of the First Causes of Morbidity or Mortality	<p>Morbidity or mortality events were defined as: a) Death; b) Atrial septostomy; c) Lung transplantation; d) Initiation of intravenous (i.v.) or subcutaneous prostanoids, or; e) Other worsening of pulmonary arterial hypertension (PAH).</p> <p>Other worsening of PAH was defined by the combined occurrence of all the following 3 events:</p> <p>At least 15% decrease in the 6 minute walk distance from baseline, confirmed by 2 tests performed on separate days, within 2 weeks.</p>	Up to end of treatment (Up to 36 months)

AND worsening of PAH symptoms including at least one of the following:

a) Increase in WHO Functional Class (WHO FC), or no change in patients in WHO FC IV at baseline; b) Appearance or worsening of signs of right heart failure that did not respond to optimized oral diuretic therapy

AND need for new treatment(s) for PAH that included the following:

a) Oral or inhaled prostanoids; b) Oral phosphodiesterase inhibitors; c) Endothelin receptor antagonists (only after discontinuation of study treatment; d) i.v. diuretics

Collaborators and Investigators

This is where you will find people and organizations involved with this study.

Sponsor ⓘ

Actelion

Investigators ⓘ

- Study Chair: Loic Perchenet, PhD, Actelion

Publications

Study Results

These publications are provided voluntarily by the person who enters information about the study and are about the study results.

- [Pulido T, Adzerikho I, Channick RN, Delcroix M, Galie N, Ghofrani HA, Jansa P, Jing ZC, Le Brun FO, Mehta S, Mittelholzer CM, Perchenet L, Sastry BK, Sitbon O, Souza R, Torbicki A, Zeng X, Rubin LJ, Simonneau G; SERAPHIN Investigators. Macitentan and morbidity and mortality in pulmonary arterial hypertension. N Engl J Med. 2013 Aug 29;369\(9\):809-18. doi: 10.1056/NEJMoa1213917. \(https://pubmed.ncbi.nlm.nih.gov/23984728\)](https://pubmed.ncbi.nlm.nih.gov/23984728/)

From PubMed

These publications come from PubMed, a public database of scientific and medical articles. This list is automatically created by ClinicalTrials.gov Identifier (NCT Number), and these articles may or may not be about the study.

- [Di Scala L, Bacchi M, Bayer B, Turricchia S. Adjusting Overall Survival Estimates of Macitentan in Pulmonary Arterial Hypertension After Treatment Switching: Results from the SERAPHIN Study. Adv Ther. 2022 Sep;39\(9\):4346-4358. doi: 10.1007/s12325-022-02253-8. Epub 2022 Aug 1. \(https://pubmed.ncbi.nlm.nih.gov/35917059\)](https://pubmed.ncbi.nlm.nih.gov/35917059/)
- [Souza R, Delcroix M, Galie N, Jansa P, Mehta S, Pulido T, Rubin L, Sastry BKS, Simonneau G, Sitbon O, Torbicki A, Boyanova N, Chamitava L, Stein C, Channick RN. Long-Term Safety, Tolerability and Survival in Patients with Pulmonary Arterial Hypertension Treated with Macitentan: Results from the SERAPHIN Open-Label Extension. Adv Ther. 2022 Sep;39\(9\):4374-4390. doi: 10.1007/s12325-022-02199-x. Epub 2022 Jul 12. \(https://pubmed.ncbi.nlm.nih.gov/35819570\)](https://pubmed.ncbi.nlm.nih.gov/35819570/)
- [Torbicki A, Bacchi M, Delcroix M, Farber HW, Ghofrani HA, Hennessy B, Jansa P, Mehta S, Perchenet L, Pulido T, Rosenberg D, Rubin LJ, Sastry BKS, Simonneau G, Sitbon O, Souza R, Wei LJ, Channick R, Benza R. Integrating Data From Randomized Controlled Trials and Observational Studies to Assess Survival in Rare Diseases. Circ Cardiovasc Qual Outcomes. 2019 May;12\(5\):e005095. doi: 10.1161/CIRCOUTCOMES.118.005095. \(https://pubmed.ncbi.nlm.nih.gov/31109190\)](https://pubmed.ncbi.nlm.nih.gov/31109190/)

- [Krause A, Zisowsky J, Dingemans J. Modeling of pharmacokinetics, efficacy, and hemodynamic effects of macitentan in patients with pulmonary arterial hypertension. Pulm Pharmacol Ther. 2018 Apr;49:140-146. doi: 10.1016/j.pupt.2018.02.005. Epub 2018 Feb 28. \(https://pubmed.ncbi.nlm.nih.gov/29501590\)](#)
- [McLaughlin VV, Hoeper MM, Channick RN, Chin KM, Delcroix M, Gaine S, Ghofrani HA, Jansa P, Lang IM, Mehta S, Pulido T, Sastry BKS, Simonneau G, Sitbon O, Souza R, Torbicki A, Tapson VF, Perchenet L, Preiss R, Verweij P, Rubin LJ, Galie N. Pulmonary Arterial Hypertension-Related Morbidity Is Prognostic for Mortality. J Am Coll Cardiol. 2018 Feb 20;71\(7\):752-763. doi: 10.1016/j.jacc.2017.12.010. \(https://pubmed.ncbi.nlm.nih.gov/29447737\)](#)
- [Jansa P, Pulido T. Macitentan in Pulmonary Arterial Hypertension: A Focus on Combination Therapy in the SERAPHIN Trial. Am J Cardiovasc Drugs. 2018 Feb;18\(1\):1-11. doi: 10.1007/s40256-017-0260-1. \(https://pubmed.ncbi.nlm.nih.gov/29280064\)](#)
- [Mehta S, Sastry BKS, Souza R, Torbicki A, Ghofrani HA, Channick RN, Delcroix M, Pulido T, Simonneau G, Włodarczyk J, Rubin LJ, Jansa P, Hunsche E, Galie N, Perchenet L, Sitbon O. Macitentan Improves Health-Related Quality of Life for Patients With Pulmonary Arterial Hypertension: Results From the Randomized Controlled SERAPHIN Trial. Chest. 2017 Jan;151\(1\):106-118. doi: 10.1016/j.chest.2016.08.1473. Epub 2016 Sep 23. \(https://pubmed.ncbi.nlm.nih.gov/27671974\)](#)
- [Simonneau G, Channick RN, Delcroix M, Galie N, Ghofrani HA, Jansa P, Le Brun FO, Mehta S, Perchenet L, Pulido T, Sastry BK, Sitbon O, Souza R, Torbicki A, Rubin LJ. Incident and prevalent cohorts with pulmonary arterial hypertension: insight from SERAPHIN. Eur Respir J. 2015 Dec;46\(6\):1711-20. doi: 10.1183/13993003.00364-2015. Epub 2015 Oct 22. \(https://pubmed.ncbi.nlm.nih.gov/26493786\)](#)
- [Channick RN, Delcroix M, Ghofrani HA, Hunsche E, Jansa P, Le Brun FO, Mehta S, Pulido T, Rubin LJ, Sastry BKS, Simonneau G, Sitbon O, Souza R, Torbicki A, Galie N. Effect of macitentan on hospitalizations: results from the SERAPHIN trial. JACC Heart Fail. 2015 Jan;3\(1\):1-8. doi: 10.1016/j.jchf.2014.07.013. Epub 2014 Nov 11. \(https://pubmed.ncbi.nlm.nih.gov/25457902\)](#)

Study Record Dates

These dates track the progress of study record and summary results submissions to ClinicalTrials.gov. Study records and reported results are reviewed by the National Library of Medicine (NLM) to make sure they meet specific quality control standards before being posted on the public website.

Study Registration Dates
First Submitted ⓘ 2008-04-14
First Submitted that Met QC Criteria ⓘ 2008-04-16
First Posted (Estimated) ⓘ 2008-04-17
Results Reporting Dates
Results First Submitted ⓘ 2013-11-05
Results First Submitted that Met QC Criteria ⓘ 2014-04-03
Results First Posted (Estimated) ⓘ 2014-05-05
Certification/Extension Dates
Certification/Extension First Submitted ⓘ 2012-10-23
Certification/Extension First Submitted that Met QC Criteria ⓘ

2012-10-23

Certification/Extension First Posted (Estimated) ⓘ

2012-10-29

[HHS Vulnerability Disclosure](#)

Study Record Updates

Last Update Submitted that met QC Criteria ⓘ

2015-09-10

Last Update Posted (Estimated) ⓘ

2015-09-28

Last Verified ⓘ

2015-08

More Information

Terms related to this study

Keywords Provided by Actelion

pulmonary arterial hypertension SERAPHIN

Additional Relevant MeSH Terms

Hypertension, Pulmonary
Lung Diseases
Respiratory Tract Diseases
Pulmonary Arterial Hypertension
Substandard Drugs
Pharmaceutical Preparations
macitentan
Counterfeit Drugs