Appendix 1. RE-LY Trial Organization Committee and Investigators.

Steering committee: Stuart Connolly (co–principal investigator), Michael Ezekowitz (co–principal investigator), Lars Wallentin (co-chair), Salim Yusuf (co-chair), Jeanne Varrone (clinical trial monitor), Ralf Bilke (clinical trial monitor until March 2008), representatives of Boehringer-Ingelheim Pharmaceuticals Inc Paul Reilly and Lars-Eric Lins, Susan Wang (trial statistician) and Ellison Themeles (PHRI Project Manager), and national coordinators Rafael Diaz (Argentina), John Amerena, (Australia), Kurt Huber (Austria), Hein Heidbuchel (Belgium), Alvaro Avezum (Brazil), Dimitar Raev (Bulgaria), Stuart J. Connolly and Mario Talajic (Canada), Liu Lishen (China), Velasco Caicedo (Colombia), Petr Jansky (Czech Republic), Knud Eric Pedersen (Denmark), Lauri Toivonen (Finland), Jean-Yves Le Heuzey (France), Harald Darius and Stefan Hohnloser (Germany), John Nanas (Greece), Chu-Pak Lau (Hong-Kong), Keltai Matyas (Hungary), Prem Pais and Denis Xavier (India), David Halon and Basil S. Lewis (Israel), Giuseppe DiPasquale and Maria Grazia Franzosi (Italy), Masatsugu Hori (Japan), Sung Soon Kim (Korea), Razali Omar (Malaysia), Jesus Antonio Gonzalez-Hermosillo (Mexico), Marco Alings and Timothy Simmers (Netherlands), Pal Smith (Norway), Raul Gamboa (Peru), Antonio L. Dans (Philippines), Andrzej Budaj (Poland), Jorge Ferreira (Portugal), Patrick Commerford (South Africa), Dragos Vinereanu (Romania), Sergey Golitsyn (Russia), Ru San Tan (Singapore), Gabriel Kamensky (Slovakia), Josep Brugada (Spain), Jonas Oldgren and Lars Wallentin (Sweden), Iris Baumgartner (Switzerland), Jyh-Hong Chen (Taiwan), Supachai Tanomsup (Thailand), Cetin Erol (Turkey), Marcus Flather (United Kingdom), Michael Ezekowitz and Greg Flaker (United States), Alexander Parkhomenko (Ukraine)
Operations committee: Stuart Connolly, John Eikelboom, Michael Ezekowitz, Jonas Oldgren, Paul Reilly, Ellison Themeles, Lars Wallentin, Salim Yusuf

Data safety monitoring board: Peter Sleight (chair), George Wyse (co-chair), Lars Ryden, Peter Sandercock, Jane Collier, Emmanuel Lesaffre, David DeMets, Jack Hirsh

Central Adjudication Core Committee: Hans-Christoph Diener (co-chair), Cam Joyner (co-chair), Anke Diehl, Gary Ford, Marlene Robinson

Death included cardiovascular and non-cardiovascular deaths. Cardiovascular death included cardiac and other cardiovascular deaths.

Cardiac death included sudden cardiac death (SCD) and progressive heart failure death. SCD was considered, in patients who: (i) died suddenly and unexpectedly within 1 h of cardiac symptoms in the absence of progressive cardiac deterioration; (ii) died unexpectedly in bed during sleep; or (iii) died unexpectedly within 24 h after last being seen alive. The diagnosis of SCD required the absence of severe pump failure death with primary electromechanical dissociation. In case of SCD, specific information regarding arrhythmic event documentation (asystole, ventricular fibrillation), as well as the specific setting of recent myocardial infarction or other special condition were prespecified. Progressive heart failure death was defined as a circulatory collapse in the form of hypotension or symptoms and/or signs of congestion at rest, requiring increased medication including intravenous agents in the preceding days. Similarly, for progressive heart failure death, the specific setting associated with pump failure was described in detail in the specific form, including conditions such as previous history of heart failure, context of cardiac tamponade, or recent myocardial infarction.

Other cardiovascular death included vascular death: fatal systemic (stroke/peripheral embolism) or pulmonary embolism, or hemorrhage. Fatal embolism or hemorrhage were defined as death from any cause within 30 days of the embolic event or major/life threatening hemorrhagic event. Stroke was an acute onset of a focal neurologic deficit of presumed vascular origin lasting for ≥24 h or resulting in death. Stroke was categorized as ischemic or hemorrhagic or cause unknown (based on computed tomographic or magnetic resonance scanning or autopsy). Systemic
embolism was an acute vascular occlusion of the extremities or any organ (kidneys, mesenteric arteries, spleen, retina or grafts) and must be documented by angiography, surgery, scintigraphy, or autopsy. Major hemorrhage was defined as a reduction in the hemoglobin level of at least 20 g per liter, transfusion of at least 2 units of blood, or symptomatic hemorrhage in a critical area or organ. Life-threatening hemorrhage was a subcategory of major hemorrhage that consisted of fatal hemorrhage, symptomatic intracranial hemorrhage, hemorrhage with a decrease in the hemoglobin level of at least 50 g per liter, or hemorrhage requiring transfusion of at least 4 units of blood or inotropic agents or necessitating surgery.

Non-cardiovascular deaths were categorized into those due to cancer, trauma, respiratory failure, infection, and other specified non-cardiovascular deaths.

Other unknown/unclassified cause of death when insufficient information was available to decide on the cause of death.
Appendix 3. Baseline Variables and Interim Events during Follow-Up

Included in Univariate Analysis.

Gender (M vs F)
Age (≥71 vs <71 y)
Weight (≥82 vs <82 kg)
Waist measurement (≥mean vs <mean)
Hypertension (Y v. N)
Ventricular rate at baseline (ECG) (<60, 60–80, >80 bpm)
Ventricular paced (Y vs N)
Intraventricular conduction delay (QRS >120 ms) (Y vs N)
Left ventricular hypertrophy (voltage or non-voltage criteria)
Diabetes mellitus (Y vs N)
Hypertension (Y vs N)
Tobacco current use (Y vs N)
Alcohol consumption (Y vs N)
Previous stroke or transient ischemic attack (Y vs N)
Prior myocardial infarction (Y vs N)
Previous non-CNS systemic embolism (Y vs N)
Documented coronary artery disease (Y vs N)
Type of atrial fibrillation (permanent vs paroxysmal/persistent)
CHADS2 score (≥3 vs <3)
Heart failure (Y v. N)
NYHA class (III/IV vs I/II)
Creatinine clearance (≤45 vs >45 mL/min)

Left ventricular ejection fraction (≤40 vs >40%)

History of oral anticoagulant agent use (Y vs N)

Known cancer history (Y vs N)

Medications in use at baseline

  Dabigatran
  Aspirin
  Angiotensin converting enzyme or angiotensin renin blocker inhibiotor
  Beta blocker
  Amiodarone
  Statin
  Proton-pump inhibitor
  Long-term vitamin K antagonist therapy

Nonfatal stroke or systemic embolism during follow-up

Nonfatal myocardial infarction during follow-up

Major hemorrhage during follow-up