Dronedaroneは心房細動の患者を脳卒中から保護する

ATHENAスタディ：ATHENAスタディのpost-hoc解析において、dronedaroneは心房細動患者の脳卒中リスクを軽減することが示された

ATHENA: Dronedarone reduced the risk of stroke in patients with atrial fibrillation in post-hoc analysis of ATHENA study

ATHENA：A Trial with dronedarone to prevent Hospitalization or dEath in patieNts with Atrial fibrillation/flutter（dronedaroneを用いて心房細動／粗動患者の入院または死亡を予防するスタディ）の新たな解析の結果、dronedaroneは抗血栓薬を含む標準治療で適切に治療されている心房細動または粗動患者において脳卒中のリスクを低下させることが示された、と2008年European Society of Cardiology学会で発表された。過去のスタディではdronedaroneを標準治療に追加することにより、プラセボを追加するのと比較し、複合一次エンドポイントである心血管疾患による入院またはあらゆる原因による死亡が統計学的に有意に24%減少した(p=0.00000002)ことが示された。今回のスタディでは、75歳以上の患者（心血管リスクファクターの有無にかかわらず）、または心房細動／粗動に加え心血管リスクファクター（高血圧、糖尿病、脳血管イベントの既往、左房サイズ>50mmまたは左室駆出率<40%）をひとつ以上有する70歳超の患者4,628人をdronedarone 400mgを1日2回またはプラセボ内服群に無作為に割り付けた。このnon-prespecified二次エンドポイントに関する脳卒中post-hoc解析の結果、dronedaroneは脳卒中（虚血性または出血）のリスクをプラセボと比較し34%低下させた（脳卒中イベントそれぞれ46件 対 70件、p=0.027）。この効果はスタディの早期に認められ、経過観察期間中維持された（12～30ヵ月）。

Full Text

The results of a post-hoc analysis of the data from the ATHENA study were presented at the clinical trial update session of the European Society of Cardiology Congress 2008, in Munich, Germany. Previous results from the landmark ATHENA study have shown that the investigational medicine dronedarone on top of standard therapy decreased the combined primary endpoint of the risk of cardiovascular hospitalizations or death from any cause by a statistically significant 24% (p=0.00000002) as compared to placebo.

The ATHENA stroke post-hoc analysis on non-pre-specified secondary endpoints showed that dronedarone decreased the risk of stroke (ischemic or hemorrhagic) compared to placebo by 34% (46 vs. 70 stroke events respectively; p=0.027) in atrial fibrillation / atrial flutter patients adequately treated by standard therapy including antithrombotics. The significant reduction in stroke risk with dronedarone was incremental to background anti-thrombotic therapy like oral anticoagulants and / or anti-platelet agents. Similar to the ATHENA primary endpoint of CV hospitalizations or death, this effect appeared early and was maintained during the study follow-up (12 to 30 months).

"ATHENA is a landmark trial that will lead to a paradigm shift in the management of atrial fibrillation as it is the first time that an anti-arrhythmic drug has shown a significant impact on cardiovascular outcomes. As stroke is one of the leading complications of atrial fibrillation, and a major cause of death and long-term disability, these new results demonstrate the unique profile of dronedarone beyond its pure rhythm and rate-controlling effects," said Professor Stuart Connolly, Mc Master University, Department of Cardiology, Hamilton Canada, co-principal investigator of the ATHENA study.

The most frequently reported adverse events of dronedarone vs. placebo in the ATHENA trial as seen in the pre-specified safety analysis, were gastrointestinal effects (26% vs. 22%), skin disorders (10% vs. 8%, mainly rash) and a mild increase in blood creatinine (4.7% vs. 1%) due to inhibition of tubular secretion of creatinine in the kidneys. The mechanism of blood creatinine increase was well defined in a separate study of healthy volunteers. In the ATHENA trial, compared to placebo, dronedarone showed a low risk of pro-arrhythmia and no excess of hospitalizations for congestive heart failure. There was a similar rate of study drug discontinuation between the 2 study groups.

The landmark ATHENA study is the only double-blind, anti-arrhythmic, morbidity-mortality study in patients with atrial fibrillation. It was conducted in more than 550 sites in 37 countries and enrolled a total of 4,628 patients.

The patients studied in ATHENA were either 75 years of age or older (with or without cardiovascular risk factor) or above 70 years of age with at least one additional cardiovascular risk factor (hypertension, diabetes, previous cerebrovascular event, left atrium size greater than 50 mm or left ventricular ejection fraction lower than 40%). Patients were randomized to receive dronedarone 400 mg BID or placebo, with a maximum follow-up of 30 months.

The ATHENA study objectives were to show a potential benefit of dronedarone on the primary composite endpoint of all-cause mortality combined with cardiovascular hospitalization as compared to placebo. The pre-specified secondary endpoints were death from any cause, cardiovascular death and hospitalization for cardiovascular reasons. The pre-specified safety endpoint was the incidence of treatment emergent adverse events (between first study drug intake and last study drug intake plus 10 days) including: all adverse events, serious adverse events, adverse events leading to study drug discontinuation.

The ATHENA stroke post-hoc analysis on a non-pre-specified secondary endpoint was conducted in order to confirm the consistent benefit of dronedarone in atrial fibrillation or atrial flutter patients in reducing major cardiovascular complications like stroke, which is a leading cause of cardiovascular hospitalizations or death in this patient population.