AVERROESトライアルは早期に中止された

AVERROES：Apixabanは出血のリスクなく脳卒中を有意に減少させる

AVERROES: Apixaban associated with significant reductions in stroke with no bleeding risk

Phase III AVERROES（脳卒中予防におけるapixaban対アセチルサリチル酸[ASA]の比較：Apixaban Versus Acetylsalicylic acid [ASA] to Prevent Strokes）トライアルは、心房細動患者においてapixabanがアスピリンと比較し臨床的に重要な脳卒中および全身塞栓症を減少させ安全性が許容範囲内であることが明らかとなったため早期に中止された。AVERROESは、ビタミンK拮抗薬（ワルファリン）治療に適さないことが示されたかまたは想定される患者5,600人（平均年齢70歳）を組み入れた二重盲検無作為化トライアルである。中間解析で脳卒中または全身塞栓症の年間発現率（一次エンドポイント）はアスピリン群で3.9%であり、apixaban群で1.7%であった（HR 0.45、P<0.001）。重大な出血の年間発現率はアスピリン群で1.4%、apixaban群で1.6%であった（HR 1.18、P=0.33）。出血性脳卒中は両群ともに年0.2%であり肝毒性または他の重大な有害事象は認められなかった。Apixabanの有益性は出血増加という代償を伴うものではなかった。このスタディ結果は、2010年European Society of Cardiology学会のホットラインセッションで発表された。

Full Text

The phase 3 AVERROES (Apixaban Versus Acetylsalicylic acid (ASA) to Prevent Strokes) trial, designed to show the superiority of apixaban over aspirin for the prevention of stroke or systemic embolism in high-risk atrial fibrillation patients unsuitable for treatment with a vitamin K antagonist (warfarin), was terminated early following a recommendation from the Data Monitoring Committee. Final study visits took place between 1 July and 15 August this year. The study results were presented during a Hotline session at ESC Congress 2010.

A predefined interim analysis had shown clear evidence of a clinically important reduction in stroke and systematic embolism and an acceptable safety profile for apixaban compared to aspirin. The principal investigator, Dr. Stuart Connolly from Population Health Research Institute, McMaster University, Hamilton, Ontario, Canada, and the study's sponsors accepted the recommendation to terminate the trial.

AVERROES was a double-blind randomized trial which recruited 5600 patients with atrial fibrillation (mean age 70 years) demonstrated or expected to be unsuitable for treatment with a vitamin K antagonist (because of difficulty in controlling treatment effect, increased risk of hemorrhage, patient refusal to take warfarin or intermediate stroke risk). So far, aspirin is the only effective treatment for stroke prevention in patients unsuitable for warfarin.

Apixaban, a Factor Xa inhibitor, has already been investigated for the prevention of deep vein thrombosis, following orthopedic surgery, and after acute coronary syndrome - but not so far in patients with atrial fibrillation. The AVERROES trial compared the effects of apixaban and aspirin in these patients. Another trial, ARISTOTLE (not yet completed) is studying apixaban against warfarin in patients suitable for warfarin.

The AVERROES study was performed at 520 sites worldwide and recruitment was completed in December 2009. The primary endpoint was a composite of stroke or systemic embolism, while the primary safety endpoint was major hemorrhage. Secondary and tertiary endpoints were a composite of stroke, systemic embolism, myocardial infarction or vascular death, and total death.

At the interim analysis results showed that the annual rate of stroke or systemic embolism (the primary outcome) was 3.9% per year on aspirin and 1.7% per year on apixaban (HR 0.45, p<0.001). The rate of major hemorrhage was 1.4% per year on aspirin and 1.6% per year on apixaban (HR 1.18, p=0.33). The rate of hemorrhagic stroke was 0.2% per year in both treatment groups and there was no evidence of hepatic toxicity or other major adverse events. The benefits of apixaban did not come at a cost of increased bleeding.

Commenting on the results, Dr. Connolly said: "The results of AVERROES are truly impressive. The reduction in stroke and systemic embolism is very important and the increased risk of hemorrhage is small. It appears that apixaban will be an excellent treatment for the many patients with atrial fibrillation who are unsuitable for warfarin. These findings will reduce the burden of stroke in society."

Conference News