実臨床においてリバーロキサバンは安全性および有効性試験をパスした (ESC2015 Presentation # 5072)

XANTUS：脳卒中予防目的でリバーロキサバンを投与された心房細動患者において出血および脳卒中発現率が低い

XANTUS: Low bleeding and stroke rates in patients with atrial fibrillation given rivaroxaban for stroke prevention

脳卒中予防目的でリバーロキサバンを投与されている心房細動（AF）患者は、出血や脳卒中の発現率が低いとのXANTUSスタディの実臨床におけるデータが2015年ESC Congressで発表された。この単一群観察研究では、日常臨床における非弁膜症性AF患者6,784人の脳卒中予防に対するリバーロキサバンの安全性および有効性を評価した。全ての治療および用量決定は治療担当医の裁量に委ねられ、患者は1年間または早期中止例ではその30日後まで追跡された。観察期間終了までに、大多数の患者（96.1%）は治療中の大出血、全死亡、脳卒中または全身性塞栓症を認めなかった。治療中の全死亡は1.9%／年であった。全体で、治療中の大出血は2.1%／年に認められ、これらの症例の多くが標準的な臨床的尺度を用いて治療された。致死的出血は0.2%／年であり、脳卒中は0.7%／年に発現した。この結果からROCKET AFの第III相試験データが確証され、直接第Xa因子阻害薬リバーロキサバンを用いた抗凝固療法は、AF患者における脳卒中予防において血栓塞栓イベントの高および低リスクの両方に対して安全で有効であることが示された。

Full Text

Atrial fibrillation (AF) patients treated with rivaroxaban for stroke prevention have low rates of bleeding and stroke, reveals real-world data from the XANTUS study presented at ESC Congress 2015. The findings confirm clinical trial data and demonstrate that oral anticoagulation with rivaroxaban, a direct Factor Xa inhibitor, is safe and effective for stroke prevention in patients with AF at both high- and low-risk of thromboembolic events.

"With 10 million people in Europe alone affected by AF, a number that is only expected to increase, real-world insights on routine anticoagulation management in everyday clinical practice is increasingly important for physicians and patients with AF," said XANTUS principal investigator Professor A. John Camm, professor of clinical cardiology in the Cardiovascular and Cell Sciences Research Institute at St George's University of London, UK.

XANTUS is the first international, prospective real-world non-vitamin K antagonist oral anticoagulant (NOAC) study in patients with AF. These patients are five times more likely than the general population to have a stroke. However, oral anticoagulation therapy can prevent many cases of AF-related stroke.

This single-arm, observational study evaluated the safety and effectiveness of rivaroxaban for stroke prevention in 6 784 patients with non-valvular AF from 311 centers across Europe and Canada in routine clinical practice. All treatment and dosing decisions were at the discretion of the treating physicians and patients were followed up for one year or until 30 days after premature discontinuation. Bleeding events and major thromboembolic events were centrally adjudicated by an independent committee.

By the end of the observation period the majority (96.1%) of patients had not experienced treatment-emergent major bleeding, all-cause death or stroke / systemic embolism. The rate of on-treatment all-cause mortality was 1.9% per year. Overall, 2.1% of patients per year experienced treatment-emergent major bleeding and most of these cases were treated using standard clinical measures. The rate of fatal bleeding was 0.2% per year, while stroke occurred in 0.7% patients per year, and critical organ bleeding occurred at a rate of 0.7% per year with 0.4% per year of patients experiencing an intracranial hemorrhage.

"These results demonstrate low rates of both major bleeding and stroke in patients taking rivaroxaban in routine clinical practice," said Professor Camm. "The findings reaffirm the positive benefit-risk profile of rivaroxaban established in the phase III clinical trial ROCKET AF, in which rivaroxaban was shown to provide effective stroke prevention with a similar overall bleeding profile and significantly lower rates of the most feared intracranial and fatal bleeds compared with vitamin K antagonists (VKAs)."

He continued: "The patients included in ROCKET AF were at moderate to high risk of stroke with a mean CHADS2 score of 3.5, and the incidence of major bleeding in those taking rivaroxaban was 3.6 per 100 person-years. In XANTUS, patients seen in daily clinical practice had a lower risk of stroke with a mean CHADS2 score of 2.0 and the incidence rate of major bleeding was lower at 2.1 per 100 person-years."

Furthermore, XANTUS showed that the majority of patients (80%) persisted on their treatment with rivaroxaban throughout the one-year study period, whereas other recent data on VKAs has shown a persistence rate of 62% after one year. "Treatment persistence is especially important as discontinuation of anticoagulation leaves patients with AF unprotected from the risk of stroke," said Professor Camm.

He concluded: "These real-world insights from XANTUS complement and expand on what we already know from clinical trials, and provide physicians with reassurance to prescribe rivaroxaban as an effective and well-tolerated treatment option for the broad range of patients with AF seen in their everyday clinical practice."

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Professor Camm has acted as a consultant for AstraZeneca, Bayer HealthCare, Boehringer Ingelheim, Bristol-Myers Squibb, Daiichi Sankyo, Pfizer, Sanofi, Aryx, and Johnson & Johnson. Other co-authors report the following: Pierre Amarenco has acted as a consultant for Bayer HealthCare Pharmaceuticals, Bristol-Myers Squibb, Pfizer, Boehringer Ingelheim, Daiichi Sankyo, AstraZeneca, Sanofi, Boston Scientific, Edwards, Lundbeck, Merck, and Kowa Pharmaceutical. Sylvia Haas has acted as a consultant for Bayer HealthCare Pharmaceuticals, Boehringer Ingelheim, Bristol-Myers Squibb, Daiichi Sankyo, Pfizer, and Sanofi. Paulus Kirchhof has received consulting fees and honoraria from 3M Medica, MEDA Pharma, AstraZeneca, Bayer HealthCare, Biosense Webster, Boehringer Ingelheim, Daiichi Sankyo, German Cardiac Society, Medtronic, Merck, MSD, Otsuka Pharma, Pfizer/Bristol-Myers Squibb, Sanofi, Servier, Siemens, and Takeda. Alexander G.G. Turpie has been a consultant for Bayer HealthCare, Janssen Pharmaceutical Research & Development, Astellas, Portola, and Takeda. Susanne Hess, Silvia Kuhls and Martin van Eickels are employees of Bayer HealthCare Pharmaceuticals.

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