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各 位

興 和 株 式 會 社

**高コレステロール血症治療剤「ピタバスタチン」
HIV 患者を対象とした今後のランドマークとなる
心疾患抑制を検討する REPRIEVE 試験の実施について**

興和株式会社（本社：愛知県名古屋市、社長：三輪芳弘）の米国における医療用医薬品販売子会社「Kowa Pharmaceuticals America, Inc.」（本社：米国アラバマ州、社長：Ben Stakely）は、このたび、米国国立衛生研究所（National Institutes of Health：NIH）の傘下機関である米国国立心肺血液研究所（National Heart Lung and Blood Institute：NHLBI）が、高コレステロール血症治療剤のピタバスタチン 4mg/日を用いて、HIV 患者の心血管疾患の一次予防を目的とした、数百万ドル規模のランドマークとなる REPRIEVE 試験（Randomized Study to Prevent Vascular Events in HIV）の実施を決定したことを発表しました。REPRIEVE 試験は HIV 患者を対象とした心疾患抑制を検討する今後のランドマークとなるアウトカム試験で、ピタバスタチンは本試験の試験薬として採用されました。

REPRIEVE 試験は、ピタバスタチンの 1 日 1 回投与が HIV 患者において心血管イベントのリスクを軽減できるかを検討する研究で、Kowa Pharmaceuticals America, Inc. が NHLBI に対して、試験薬の提供ならびに試験に係る一部追加費用を支援いたします。また National Institute of Allergy and Infectious Diseases (NIAID)、AIDS Clinical Trials Group (ACTG) の関連施設が本試験のサポートを行います。

本無作為化、二重盲検比較試験では、6 年の試験期間、約 100 施設から 6,500 名の登録を計画しております。そして REPRIEVE 試験の研究代表者は、Steven Grinspoon 医師（Director of the Massachusetts General Hospital、Program in Nutritional Metabolism and professor of Medicine at Harvard Medical School）、研究副代表を Pamela Douglas 医師（Professor of Medicine at Duke University School of Medicine）、Udo Hoffmann 医師（Professor of Radiology at Harvard Medical School）、Heather Ribaldo 博士（Senior Biostatistician at Harvard School of Public Health）が務めます。

この大規模臨床試験の実施により、HIV 患者の血管イベント予防法としての確立が期待できます。

全世界で約 3,400 万人、全米で 170 万人が HIV に感染しており、最近の研究では HIV 感染患者は一般の人々と比べて 50~100%の割合で心血管疾患の発症率が高いことが指摘されておりますが、現在このような患者に対する治療法は確立されていません。^{1~6}

詳細につきましては、Kowa Pharmaceuticals America, Inc.が発表したプレスリリースをご参照ください。

■ REPRIEVE 試験 概要

試験名	HIV 患者の血管イベント予防効果を検証する無作為化試験 (REPRIEVE)
目的	HIV 患者における心血管疾患の一次予防法の確立
対象	40 歳から 75 歳までの HIV 患者
症例数	6,500 名
試験薬	ピタバスタチンまたはプラセボ
試験期間	6 年間
1 次エンドポイント	主要心血管イベント
参加施設数	約 100 施設

- ¹ Global Report: UNAIDS Report on the Global AIDS Epidemic 2012 Saturday, 1 December, 2012; <http://www.avert.org/worldwide-hiv-aids-statistics.htm>
- ² UNAIDS Gap Report 2014; UNAIDS Fact Sheet 2014; U.S. Centers for Disease Control and Prevention; <http://www.amfar.org/about-hiv-and-aids/facts-and-stats/statistics--united-states/>
- ³ Lang S, Mary-Krause M, Cotte L, et al. Increased risk of myocardial infarction in HIV-infected patients in France, relative to the general population. *AIDS*. 2010; 24:1228-1230.
- ⁴ Triant VA, Lee H, Hadigan C, Grinspoon SK. Increased acute myocardial infarction rates and cardiovascular risk factors among patients with human immunodeficiency virus disease. *J Clin Endocrinol Metab*. 2007; 92:2506-2512.
- ⁵ Obel N, Thomsen HF, Kronborg G, et al. Ischemic heart disease in HIV-infected and HIV-uninfected individuals: a population-based cohort study. *Clin Infect Dis*. 2007; 44:1625-1631.
- ⁶ Freiberg MS, Chang CC, Kuller LH, et al. HIV infection and the risk of acute myocardial infarction. *JAMA Intern Med*. 2013; 173:614-622.

■ お問い合わせ先

- ・ REPRIEVE 試験に関するお問い合わせ先

info@KowaPharma.com (日本語対応可)

ご質問は Kowa Pharmaceuticals America, Inc.を通じて Massachusetts General Hospital (MGH) に送られ、MGH より回答が送られます。

- ・ プレスリリースに関するお問い合わせ先

興和株式会社 広報第二部

TEL : 03-3279-7392



Lisa Garman

Kowa Pharmaceuticals America, Inc.
Mobile (334) 296-1917
lgarman@kowapharma.com

**LANDMARK TRIAL TO EXPLORE THE PREVENTION OF HEART DISEASE IN PEOPLE
LIVING WITH HIV**

Trial will evaluate if a daily dose of the statin, pitavastatin, can reduce the elevated risk of cardiovascular disease in this patient population

MONTGOMERY, AL, October 28, 2014 – The National Institutes of Health (NIH)/National Heart, Lung and Blood Institute (NHLBI) are initiating a landmark multimillion dollar outcomes trial utilizing pitavastatin for the primary prevention of cardiovascular disease (CVD) in persons infected with HIV. The REPRIEVE (Randomized Study to Prevent Vascular Events in HIV) study will investigate whether a daily dose of pitavastatin will reduce the risk of CVD in people living with HIV. Kowa Pharmaceuticals America, Inc. will provide support by donating the study drug and additional study funds. The nationwide study is sponsored by the National Heart, Lung and Blood Institute (NHLBI), part of the National Institutes of Health (NIH), with additional resources and collaboration from the National Institute of Allergy and Infectious Diseases (NIAID) and the AIDS Clinical Trials Group (ACTG) Network.

The randomized, double-blind clinical trial will span six years and include 6,500 participants from approximately 100 trial sites in North America. Steven Grinspoon, M.D., Director of the MGH Program in Nutritional Metabolism and Professor of Medicine at Harvard Medical School, will lead the REPRIEVE trial, with Co-Principal Investigators Pamela Douglas, M.D., Professor of Medicine at Duke University School of Medicine, Udo Hoffmann, M.D., M.P.H, Professor of Radiology at Harvard Medical School and Heather Ribaud, Ph.D., Senior Biostatistician at Harvard School of Public Health. Additional study leadership includes Turner Overton, M.D., University of Alabama (Co-Chair), Carl Fichtenbaum, M.D., University of Cincinnati (Vice Chair), Judy Aberg, M.D., Mt. Sinai School of Medicine (Vice Chair), Markella Zanni, M.D., Massachusetts General Hospital (Vice Chair).

Study participants – HIV-infected men and women, ages 40-75, who are being treated for their infection and who have no known cardiovascular disease and low traditional risk factors for cardiovascular disease – will be randomized to receive either a 4 mg daily dose of pitavastatin or a placebo pill for up to 72 months. Within the larger group of 6,500 participants, 800 will also receive detailed assessments of the impact of pitavastatin treatment on the characteristics of arterial plaques and on biomarkers of inflammation in order to identify the mechanisms behind the effects of statin therapy in the primary prevention of CVD in this randomized, double-blind study.

An estimated 34 million people globally and 1.7 million Americans live with HIV, and recent data suggest that HIV-infected people have a 50- to 100-percent greater likelihood of developing cardiovascular disease compared with the general population. Importantly, there are no current

treatment options that have been able to successfully demonstrate prevention of CVD in this population.

“The risks of heart attack and stroke in HIV-infected individuals are significantly higher than they are in uninfected people, and while some of these patients have traditional cardiovascular risk factors, recent studies suggest that HIV infection itself confers a unique set of risks, including immune system activation and arterial inflammation. Those findings contributed to the hypothesis that statin therapy – which reduces inflammation and immune activation, as well as lipid levels – may be particularly well tailored to reducing that cardiovascular risk,” says Dr. Grinspoon. “REPRIEVE will be among the largest randomized clinical trials conducted in the HIV population and the first study designed to investigate a large-scale cardiovascular disease prevention strategy in this population. By addressing the critical question of statin efficacy in this group of patients, the study should provide important information as to efficacy and safety of this strategy for primary cardiovascular disease prevention in this population.”

“We are very excited that pitavastatin was selected for this NIH/NHLBI sponsored landmark outcomes trial in a growing population at considerable risk for cardiovascular disease,” said Craig Sponseller, M.D., Vice President of Medical Affairs at Kowa Pharmaceuticals America, Inc. “We are pleased to be able to support this important trial which we hope will lead to the first successful prevention strategy for cardiovascular disease in HIV-infected patients.”

The study is being funded through NHLBI grants U01HL123336 (clinical coordinating center) and U01HL123339 (data coordinating center). The AIDS Clinical Trials Group is funded through NIAID grants UM1 AI068636, UM1 AI106701, and UM1 AI068634.

About Kowa Company, Ltd. and Kowa Pharmaceuticals America, Inc.

Kowa Company, Ltd. (Kowa) is a privately held multinational company headquartered in Nagoya, Japan. Established in 1894, Kowa is actively engaged in various manufacturing and trading activities in the fields of pharmaceuticals, life science, information technology, textiles, machinery and various consumer products. Kowa's pharmaceutical division is focused on research and development for cardiovascular therapeutics (dyslipidemia, type 2 diabetes and atherosclerosis), ophthalmology and anti-inflammatory agents.

Kowa Pharmaceuticals America, Inc., headquartered in Montgomery, AL, is focused primarily in the area of cardiometabolic diseases. Established in September 2008, Kowa Pharmaceuticals America focuses its efforts on the successful commercialization of its current and near-term portfolio of pharmaceutical products, and business development activities.

For more information about Kowa Pharmaceuticals America, visit www.kowapharma.com.