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Stage

Clinical studies in healthy adults: Completed for the following 3 combinations, i.e.
1. Febuxostat + Inosine,
2. Topiroxostat + Inosine and
3. Allopurinol + Inosine

A clinical study in 2 patients with mitochondrial disease: Completed
A clinical study in 26 PD patients: Completed

Intellectual Properties

All patents are owned by StaGen
1st patent: Approved in 6 countries including Japan, U.S., China, Europe, and other countries.
2nd patent: approved in the U.S., Japan, China, and Europe
Use patent for the treatment of PD: approved in Japan
Anti-aging and life extension patent: joint application with Tokyo Women's Medical University

The superiority of our drugs

Our patents cover different combinations of XOR inhibitors and inosine, whether administered concurrently, as a kit formulation, or as a combination product,

Overview of ATP (energy) enhancer with anti-aging effect

StaGen Co., Ltd. is developing an anti-aging and life-extension drug called ATP enhancer. ATP enhancer is a concomitant treatment with febuxostat (XOR inhibitor) and inosine, or a combination drug containing the two compounds, and the patents have been approved in Japan, the United States, China, Europe, and other countries. Both animal studies and clinical data have shown beneficial effects.

Mitochondrial protection and lifespan extension in nematodes

There are various theories about the cause of aging, but it is believed that mitochondria, the ATP (energy) production factories, deteriorate with age, and the resulting reactive oxygen release causes various abnormalities. In a joint study with Tokyo Women's Medical University, low concentrations of febuxostat prevented mitochondrial deterioration due to aging in nematodes and extended their lifespan by enhancing ATP[1]. However, those effects disappeared at high concentrations since a reactive oxygen scavenger urate decreased. The lifespan extension was restored by adding anti-reactive oxygen substances such as urate[1]. Disease improvement effects were shown in nematode models of AD and PD by the co-administration of febuxostat and reactive oxygen suppressants[1].

Proved improvement effects for AD and PD in clinical studies

The brain is the most important organ for aging, and AD and PD are diseases caused by brain aging. No satisfactory drugs are available for AD or PD. Based on our discovery using outstanding technologies, we filed patents for the treatments of AD and PD by ATP enhancement by a co-administration of febuxostat and inosine or a combination drug[2]. After our patent application, as expected, a paper was published by US researchers using AI that febuxostat was the most effective for AD among all drugs[3]. Further, by clinical big data analyses in Taiwan[4], Germany[5], the US[6], and Korea[7], it was reported that XOR inhibitors febuxostat and allopurinol suppress the onset of dementia including AD. However, febuxostat alone is not effective enough and has a risk of hypouricemia[2]. The combination drug of febuxostat and inosine completely solves these problems. We proved that the combination therapy was far superior to the monotherapy in a clinical trial[9]. The safety of the combination therapy has already been confirmed in 65 people. In a clinical trial for 26 PD patients, the primary endpoint of MDS-UPDRS Part 3 was significantly improved along with a remarkable increase in the ATP precursor hypoxanthine[8].

Frequencies of diseases related to aging and the critical significance of the drug development

Aging affects many organs, but brain aging is the biggest problem. In the US, 6.7 million people suffer from AD, and 1 million suffer from PD. These numbers will surely increase in the future because of the aging of the population. The development of drugs for AD and PD is, therefore, an urgent issue. Many researchers believed that the cause of AD and PD is the accumulation of abnormal proteins and several drugs to reduce abnormal proteins have been developed. However, their effects have been limited, if any. By analyzing a vast amount of genomic, clinical, and evolutionary data, we have elucidated that cellular ATP (energy) deficiency caused by mitochondrial dysfunction is the most upstream abnormality and that simultaneous administration of an XOR inhibitor and inosine improved the deficiency. Recent mounting evidence both from clinical and basic fields has increasingly supported our hypothesis. The efficacy of XOR inhibitors applies to aging in organs other than the brain. We believe that those abnormalities will also be ameliorated by our treatment.

Current status and future plans

First, we start the treatment of AD and PD patients with combination therapy of the generic drug febuxostat and the supplement inosine for off-label use. Once development funds are obtained, GMP-grade inosine tablets will be manufactured and used. The development of new drugs for mitochondrial disease or AD will be started as a combination drug when possible. In addition, we can also develop combination drugs for AD and dementia.

Reference

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Biography of Naoyuki Kamatani,MD, PhD

NK graduated from the University of Tokyo Faculty of Medicine in 1973.

From April 1979 to March 1982, he worked as a post-doctoral fellow at the Scripps Research Institute in California, USA, where he discovered MTAP deficiency in human cancers that led to the first report of a cancer suppressor gene, and proposed the world's first personalized cancer treatment.

From 1998 to 2008, he served as Director of the Institute of Rheumatology, Tokyo Women's Medical University.

From April 1989 to March 1990, he was a Visiting Professor of Internal Medicine at the University of Michigan, USA.

From April 2010 to December 2011, he served as Director of the RIKEN Center for Genomic Medicine, where he led genome-wide association studies (GWAS) of various diseases. He has authored more than 600 papers, including 34 in Nature and Nature Genetics.