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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 MD patients: Completed

A clinical study in 26 PD patients: Completed

Intellectual Property

All patents are owned by StaGen

Takaha Pharma will be granted a license from StaGen Co. Ltd.

Combination drug patents: Approved in Japan, the U.S., China, Europe, and others.

The superiority of our drugs:
Our drugs have a unique, clear clinically proven mechanism of action. The success rate is very high since the two compounds in each combination drug have been widely used, big-data analyses have confirmed the efficacies on AD, dementia and PD, and the target is narrowed to the surely effective low Hypo PD segment.

Takaha Pharma's challenge

Takaha Pharma is developing new drugs, ATP enhancers each of which is a combination drug of an XOR inhibitor (e.g. febuxostat) and inosine, for Parkinson's disease (PD), Alzheimer's disease (AD), dementia and mitochondrial disease (MD)[1]. The combination drugs are patented in Japan, the US, China, Europe, etc, and evidence for safety and efficacy has been obtained in clinical trials for PD and MD.

Confirmed clinical effects of XOR inhibitors on AD and PD

We have discovered that cellular ATP (energy) deficiency is an upstream cause of AD and PD by analyzing big genomic and evolutionary data. We also discovered that simultaneous administration of an XOR inhibitor and inosine enhances ATP by increasing hypoxanthine (Hypo), and filed for patents for the combination drugs[1]. After our patents, clinical big data analyses in Germany[2], US[3], and Korea[4] showed that the XOR inhibitors febuxostat and allopurinol prevented dementia and AD. A meta-analysis[5] confirmed the result. In addition, a recent AI study showed that febuxostat is the most effective to prevent AD[6] Another big data analysis confirmed that an XOR inhibitor prevented PD[7]. However, XOR inhibitors alone have problems of inadequate efficacy, risk of hypouricemia, and the expiration of substance patents. Our patents for the combination drugs solve those three problems[1]. We have already confirmed the safety and efficacy of the combined treatment for MD[8] and PD[9] in clinical trials and published papers. Hypo is low in PD and AD, and our treatment is more effective in patients with lower Hypo[10]. First, we develop a combination drug of febuxostat and inosine targeting PD with low Hypo to increase the success rate of our drug development project. In the future, we will also develop drugs for other diseases.

Safety and efficacy confirmed by clinical trials

ATP enhancer has been developed by the simultaneous administration of febuxostat and inosine. It has been administered to 65 individuals (18 healthy subjects and 47 patients) and the safety was confirmed. In healthy subjects, the administration for 2 weeks significantly increased ATP and Hypo, whereas either compound alone increased them only little[10]. A biomarker of heart failure (BNP) was dramatically improved in a mitochondrial cardiomyopathy patient, and a biomarker of diabetes (insulinogenic index) was dramatically improved in a mitochondrial diabetes patient[8]. Furthermore, treatment of 26 Parkinson's disease patients with febuxostat and inosine for 8 weeks resulted in a significant improvement ($P = 0.0146$) in MDS-UPDRS Part III scores with more than the minimum clinically important difference (MCID = -3.25)[9].

Disease frequencies and significance of our new drugs

Because of the aging of the population, the number of PD patients is expected to be about 30 million in 2030 worldwide. The number of dementia patients including AD will be much more. However, no disease-modifying drugs are available for PD. Many researchers and pharmaceutical companies believed that PD is caused by the accumulation of α-synuclein, and drugs have been developed to reduce this protein. However, the results of clinical trials have been disappointing. Through the analysis of vast amounts of genomics, omics, and evolutionary data, we have discovered that ATP deficiency due to mitochondrial dysfunction is upstream of the abnormal protein accumulation in PD and AD. Recently, an injectable drug has been reported to be effective in a clinical trial for AD. However, besides AD, there is another type of dementia due to impaired blood flow that supplies oxygen and glucose necessary for ATP production. Our drug is expected to be effective for both. An oral drug that is effective for both vascular dementia and AD as well as PD is of great significance.

Current status and future plans for the development

Contact stability for the combination drug of febuxostat and inosine was confirmed. We plan a phase Ib trial enrolling 24 PD patients to find optimal doses, combination ratio of the two compounds and target segments. The results of the phase Ib trial will determine whether we proceed to phase II/III combined study or a phase II study followed by a phase III study. We are considering an IPO or M&A after the completion of the phase III trial in 2029. We are currently seeking additional capital of $5 M for the phase Ib trial.

References

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Biography of Naoyuki Kamatani,MD, PhD, CEO of Takaha Pharma

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.