



**Press Release (2017/03/21)**

**Efficacy and Blood Plasmalogen Changes by Oral Administration of Plasmalogen  
in Patients with Mild Alzheimer's Disease and Mild Cognitive Impairment:  
A Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial**

### Background

Plasmalogens (PIs) reportedly decreased in postmortem brain and in the blood of patients with Alzheimer's disease (AD). Recently we showed that intraperitoneal administration of PIs improved cognitive function in experimental animals. In the present trial, we tested the efficacy of oral administration of scallop-derived purified PIs with respect to cognitive function and blood PIs changes in patients with mild AD and mild cognitive impairment (MCI).

### Methods

The study was a multicenter, randomized, double-blind, placebo-controlled trial of 24 weeks. Participants were 328 patients aged 60 to 85 years who had 20 to 27 points in Mini Mental State Examination-Japanese (MMSE-J) score and five or less points in Geriatric Depression Scale-Short Version-Japanese (GDS-S-J). They were randomized to receive either 1 mg/day of PIs purified from scallop or placebo. The patients and study physicians were masked to the assignment. The primary outcome was MMSE-J. The secondary outcomes included Wechsler Memory Scale-Revised (WMS-R), GDS-S-J and concentration of phosphatidyl ethanolamine plasmalogens (PIsPE) in erythrocyte membrane and plasma. This trial is registered with the University Hospital Medical Information Network, number UMIN000014945.

### Findings

Of 328 patients enrolled, 276 patients completed the trial (140 in the treatment group and 136 in the placebo group). In an intention-to-treat analysis including both mild AD ( $20 \leq \text{MMSE-J} \leq 23$ ) and MCI ( $24 \leq \text{MMSE-J} \leq 27$ ), no significant difference was shown between the treatment and placebo groups in the primary and secondary outcomes, with no severe adverse events in either group. In mild AD patients, WMS-R improved significantly in the treatment group, and the between group difference was nearly significant ( $P = 0.067$ ). In a subgroup analysis of mild AD patients, WMS-R significantly improved among females and those aged below 77 years in the treatment group, and the between-group differences were statistically significant in females ( $P = 0.017$ ) and in those aged below 77 years ( $P = 0.029$ ). Patients with mild AD showed a significantly greater decrease in plasma PIsPE in the placebo group than in the treatment group.

### Interpretation

Oral administration of scallop-derived purified PIs may improve cognitive functions of mild AD.

**Published in EBioMedicine:** DOI: <http://dx.doi.org/10.1016/j.ebiom.2017.02.012>

**Correspondence to Dr. Takehiko Fujino, MD., Ph.D.,**  
Institute of Rheological Functions of Food  
2241-1 Kubara, Hisayama-machi, Kasuya-gun, Fukuoka 811-2501 Japan  
E-mail address: fujino-t@boocsclinic.com