

Grifols publishes interim results of its clinical trial on Alzheimer's disease

- **The preliminary results of the trial suggest that patients who received treatment showed a trend towards stabilization of the disease.**
- **The line of investigation was based on the systematic practice of therapeutic plasmapheresis with Human Albumin Grifols in patients with this disease.**

Barcelona, 21 September 2009.

Back in 2005, the Clinical Research Department at Grifols designed a clinical study to explore whether the use of successive plasmapheresis with human albumin in patients with Alzheimer's disease could mobilize the beta amyloid protein implicated in the disease from the cerebrospinal fluid into the blood. Dr. Boada, Medical Director of the Fundació ACE and Clinician Head at the Neurology Service at the Vall d'Hebron Hospital, Barcelona, agreed to conduct this preliminary study, and the positive results with respect to the cognitive status of the patients treated gave rise to the design and development of a clinical trial with the participation of three hospitals in Spain and two in the United States.

The interim results of this trial, recently published in the journal *Drug News and Perspectives* (DOI: 10.1358/dnp.2009.22.6.1395256) highlight both the improvement of cognitive status of patients treated and the evidence that amyloid beta is mobilized in the blood of patients who undergo therapeutic plasmapheresis with albumin. However, it is necessary to complete the clinical trial before the improved cognitive development can be confirmed.

The results published to date correspond to the trial directed by Dr. Boada which is being conducted jointly at the Vall d'Hebron Hospital (Barcelona), Gregorio Marañón Hospital (Madrid), and Fundació ACE (Barcelona), with the cooperation of the Blood and Tissues Bank of Catalonia, the Pathological Anatomy Service of the Bellvitge Hospital and the Howard University Hospital in Washington, DC, and the Mid Atlantic Geriatric Association in New Jersey, both in the United States. "It would be premature to draw definitive conclusions when we are only halfway through the trial," explains Dr. Boada, "but the results published so far are positive and promising," she concludes. Dr. J. Oliveras, Director of Clinical Trials and Pharmacovigilance at Grifols, told us that, "although we are optimistic, the potential relevance of such a trial means that we must be extremely careful and must rigorously complete the research."

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Alzheimer's disease is the major cause of dementia in the developed world, and Grifols is pursuing three other lines of investigation, including a clinical study into the use of human intravenous immunoglobulin (IVIg) in the treatment of this pathology.

Grifols' R&D area has spent years studying plasma proteins, exploring their therapeutic potential with the aim of identifying potentially effective treatments. In recent years, albumin has been the subject of a number of research lines which have led to the identification of new formulations, new purification methods or, in the case of Alzheimer's disease, potential new therapeutic applications.

About Beta Amyloid

The protein known as APP (amyloid precursor protein) is present in the human body and performs the physiological role of protecting the neurons, maintaining their development, and helping to repair them if they become damaged. Other proteins known as enzymes are involved in metabolizing this protein, which is broken down into smaller fragments. Under normal conditions, these enzymes which belong to the secretase family give rise to fragments of APP which do not have any harmful effect. However, in Alzheimer's disease the production of these fragments is anomalous, creating excessive quantities of one type of fragment, amyloid beta 42, which has a harmful effect on the neurones. This amyloid beta 42 binds together to form fibrils, and these in turn bind together to form neuritic plaques which kill the neurons by breaking the connections between them and thus destroying the neural networks responsible for behavioural, psychological and cognitive functions, all of which are altered in patients with Alzheimer's disease.

Albumin

There is consensus in identifying beta amyloid protein as one of the key elements involved in the development of Alzheimer's disease, which has such a devastating impact on our society. Studies are being conducted to explore a whole range of possible approaches to stopping this disease. Albumin is the most abundant protein found in plasma, accounting for 52%. One of its functions is to fix and transport the majority of the beta amyloid protein which circulates in the plasma, and Grifols' hypothesis was to test whether, by carrying out successive plasma replacement treatments in patients with Alzheimer's disease, it was possible to mobilize this protein and remove it from the cerebrospinal fluid. After a few sessions, the new albumin added to the bloodstream would remove the plasma beta amyloid, and the dynamic equilibrium between the plasma, the cerebrospinal fluid and the neuritic plaques would bring about the mobilization of the beta amyloid deposited in these plaques.

About plasmapheresis

Plasmapheresis is a technique used to separate plasma from other blood components such as red blood cells, platelets and other cells. When somebody donates plasma, these other components are suspended in saline solution and injected back into the donor as part of the original donation process. This ensures that the donor's recovery is rapid and complete.

In the case of therapeutic plasmapheresis, the process is similar, but most of the patient's plasma is extracted and replaced with an albumin which is used to suspend the blood cells prior to reinjection.

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The generalized use of the technique of plasmapheresis as a method of obtaining plasma is the result of research conducted by Dr. J. A. Grifols Lucas in the 1940s, which he presented at the International Transfusion Congress held in Lisbon in 1951. Professors F. Císcar Rius and P. Farreras Valentí, have argued that plasmapheresis is “Spanish science’s major contribution to medicine” (*Diagnóstico hematológico* Barcelona: Ed. Jims, 1972, t. II p. 1547).

About Alzheimer’s disease

It is believed that Alzheimer’s disease will reach epidemic proportions in the 21st century, with a relentless impact on the elderly population in developed countries.

According to the *Alzheimer’s Association*, the illness affects 10% of people over 65 and as many as 30% of those over 85. In the United States there are 4.5 million sufferers, and it has been calculated that this could rise to 15 million by 2050. The direct and indirect health costs of caring for patients are estimated at 85 billion euros per year in the United States alone.