aptaTargets makes strides in treatment for stroke patients

- Completes the first part of its clinical trial of ApTOLL in stroke patients
- An excellent safety profile has been demonstrated at four dose levels
- It will be tested with two doses on 119 more patients in Spain, France, Germany and Portugal

17 June 2021. The biotechnology company aptaTargets has completed the first part of the APRIL study, a Phase Ib / IIa clinical trial of ApTOLL, a novel and powerful immunomodulator and anti-inflammatory, capable of reducing brain damage in stroke patients.

In the first phase of the trial (Ib), 32 patients have been recruited and four dose levels have been administered and, according to preliminary data, ApTOLL has shown an excellent safety profile in patients.

The second phase of the trial (IIa) will begin immediately and is expected to end in the first quarter of 2022. Two doses of the drug will be tested on 119 more patients with the main objective of confirming its safety and providing the first efficacy data. ApTOLL has already obtained the authorization to start phase IIa from the health authorities of Spain, France, Portugal and Germany.

The first phase of the trial (Ib) has been carried out in seven hospitals in Spain: Vall d´Hebron and Bellvitge (Barcelona), Germans Trias i Pujol (Badalona), Josep Trueta (Gerona), La Princesa (Madrid), Clinic of Valladolid and Virgen del Rocío (Sevilla).

These centres will be joined by five more hospitals in Spain (Ramón y Cajal and 12 de Octubre in Madrid, La Fe in Valencia, Juan Canalejo in La Coruña and Central de Asturias), in addition to seven other hospitals in Germany, France and Portugal.

In March 2020, Phase Ia was completed at La Princesa hospital. In this study, increasing doses of the drug were administered to 46 healthy volunteers and no relevant adverse events were detected, confirming the excellent safety profile observed in preclinical studies.

New activity

ApTOLL is the only drug in development for the treatment of acute ischemic stroke that blocks the activation of TLR4, a receptor on the membrane of immune system cells, such as microglia, neutrophils, macrophages, and lymphocytes. Activation of TLR4 initiates the inflammatory cascade that leads to the death of neurons and the consequent worsening of brain injuries. Therefore, by acting as a TLR4 antagonist, ApTOLL regulates the unwanted immune response, preventing the inflammatory cascade that occurs in the first hours after the onset of stroke.

To date, no neuroprotectant has shown any efficacy in clinical trials in acute ischemic stroke patients. Current treatments focus on the recanalization of occluded arteries, via the administration of thrombolytic drugs (which dissolve the thrombus) or, more recently, by catheter removal of the thrombus (endovascular therapy or mechanical thrombectomy).

Combination with mechanical thrombectomy

Administered after stroke and combined with endovascular treatment, ApTOLL may provide important benefits for patients by slowing the growth of the brain lesion even before recanalization of the affected artery achieved. In this way, the chances of neurological recovery increase, which will directly affect the patient's quality of life. “Our treatment is a neuroprotective molecule that reduces inflammation in the acute phase of stroke. We intend to combine this neuroprotective effect with mechanical thrombectomy, a combination that is expected to generate synergistic and positive effects in patients”, explains Dr. Marc Ribó, Medical Director of aptaTargets and coordinator of the APRIL study. “In this first study, we target patients with severe strokes in whom a greater benefit is expected, but we are already planning new trials to assess the effect of ApTOLL in patients with lower stroke severity or even with cerebral hemorrhage, where inflammation also causes significant damage"

About stroke

Stroke is more a disabling than a fatal disease , being considered the leading cause of disability in adults, the second cause of death and the second cause of dementia after Alzheimer's disease, as well as the most frequent cause of Admission to neurology services and extension of hospital stay, according to *The Burden of Stroke in Europe.* The social and health consequences that it entails make it essential to rapidly develop new therapeutic strategies to slow down the evolution of the disease and to improve long-term functionality of patients.

Stroke has a high incidence, estimating an average of 200-250 cases per 100,000 inhabitants per year. In Europe, 650,000 people die every year from this disease, 40,000 in Spain where 120,000 new cases are detected annually, according to the Iberictus study and the Spanish Ictus Atlas. In Europe, it is the second leading cause of mortality after ischemic heart disease and, according to data from the Stroke Observatory and the World Health Organization, it entails annual costs of 27,000 million euros.

Ischemic-type stroke is the most common in approximately 86% of cases (vs. hemorrhagic stroke, which amounts to 14% of cases).

Other indications

In addition to neuroprotection in stroke patients, ApTOLL has also shown a significant protective effect in preclinical models of other therapeutic indications, including hemorrhagic stroke, myocardial infarction and multiple sclerosis. "Recently, a study has been published in which the inhibition of the TLR4 receptor with ApTOLL, in a model of myocardial infarction in pigs, a significant functional improvement is observed", comments Dr. Macarena Hernández, Scientific Director of aptaTargets.

About aptaTargets

Founded in 2014 by David Segarra and Maria Eugenia Zarabozo, aptaTargets span-out from Aptus Biotech, an aptamer technology platform. AptaTargets started a drug development program, in collaboration with the Complutense University and the Ramón y Cajal University Hospital. In 2017, Caixa Capital Risc and Inveready Asset Management, venture capital funds specialized in biotechnology, completed the first financing round for the company (2.7 million euros).

In June 2019, aptaTargets started clinical trials, a First-in-Human study in healthy volunteers. that was successfully completed in March 2020. ApTOLL is the first aptamer (single-stranded DNA molecule) targeting TLR4, a receptor that triggers the immune response in human subjects in the first steps of the inflammatory pathway after stroke, and in other pathologies.

The company has just closed the second round of financing, with the participation of Inveready and the CDTI, through its INNVIERTE program, which will allow it to mobilise up to 5 million euros between 2020 and 2022. With these funds, aptaTargets aims to complete a clinical proof-of-concept in acute ischemic stroke patients and close a licensing agreement.

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