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Grifols Phase 2/3 trial shows positive impact of immunoglobulin therapy on post-polio patients

- ***Study met primary endpoint, demonstrating a significant improvement in the two-minute walk distance after one year of intravenous immunoglobulin (IVIG) infusions compared to placebo***

- ***Treatment found to be safe and well-tolerated with a safety profile similar to that of IVIG administered for other indications***

- ***Grifols continues applying its deep scientific expertise in IG and other plasma medicines and healthcare solutions to help patients lead better lives***

Barcelona, Spain, March 13, 2025 – Grifols (MCE: GRF, MCE: GRF.P NASDAQ: GRFS), a global healthcare company and leading producer of plasma-derived medicines, today announced positive results from its phase 2/3 clinical trial (NCT02176863) evaluating the efficacy and safety of Grifols intravenous immunoglobulin (IVIG) to treat patients with post-polio syndrome (PPS), demonstrating a significant improvement in distance walked compared to placebo.

This study met its primary endpoint of enhanced physical performance in the two-minute walk distance (2MWD) after the one-year treatment period. Patients who received monthly IVIG infusions of 1g/kg showed a statistically significant improvement in 2MWD versus placebo. The least squares mean 2MWD change from baseline at week 52, after adjusting for differences between groups, was 12.75 meters, equating to a mean improvement of 6.07 meters over placebo.

The immunomodulatory properties of IVIG – in this case Flebogamma® 5% DIF (immune globulin intravenous [human]) – are believed to have a role in potentially improving this disabling condition.

Patients with PPS are given the 2MWD test as it provides insights into their functional mobility and physical endurance over time, from baseline to the end of treatment. This helps clinicians and researchers understand the impact of interventions on patients' daily lives, especially their ability to perform physical activities and maintain independence.

The clinical trial evaluated whether Flebogamma 5% DIF, dosed at 1g/kg, improved the physical capabilities of PPS patients compared with the placebo group, using changes in the 2MWD from baseline as the primary measure. In the majority (95%) of the 191 participants, the legs were the main part of the body impacted by PPS symptoms.

Treated patients with IVIG 1g/Kg also showed greater numerical endurance as measured by the six-minute walk distance (6MWD). The least squares mean 6MWD change from baseline at week 52, after adjusting for differences between groups, was 29.16 meters, which equates to a mean improvement of 15.8 meters over placebo.

The treatment was found to be safe and well-tolerated with a similar safety profile to that of IVIG administration in other indications.

PPS can emerge decades after an initial polio infection. Symptoms – including chronic fatigue, joint and muscle pain, persistent and progressive muscle weakness and atrophy – typically develop 30 to 40 years after the initial paralytic attack and tend to worsen over time.[1] Muscle deterioration can lead to functional decline and impaired mobility, limiting patient autonomy and significantly impacting quality of life.

Worldwide, an estimated 12-to-20 million polio survivors face the risk of developing PPS symptoms.[2] Between 25% and 40%[3] of them will likely develop the condition later, representing a substantial unaddressed healthcare gap.[4]

PPS remains under researched. There are no medications indicated for the syndrome, and therapies are limited to supportive measures such as orthoses and other assistive devices, as well as symptom management.

“These results show a meaningful physical accomplishment, providing patients with more freedom of movement and the ability to be more self-reliant,” said Dr. Jörg Schüttrumpf, Grifols Chief Scientific Innovation Officer. “Grifols is committed to increasing the range of indications of its plasma-derived medicines and other biopharmaceuticals to benefit more patients globally and make a real positive difference in their lives.”

“This study is great news since it proves that the ongoing decline in physical functioning due to post-polio syndrome, which was so far considered inevitable, can be halted, and even be improved, said Dr. Frans Nollet, of the Department of Rehabilitation Medicine of the Academic Medical Center, University of Amsterdam, and one of the study’s principal investigators. “That is positive for all polio survivors, who are confronted with increasing disabilities as they age and for whom no effective medication was yet available.”

About Flebogamma® 5% DIF

Flebogamma® 5% DIF is an immune globulin intravenous (human) solution indicated in adults and pediatric patients 2 years of age and older for the treatment of primary immunodeficiency (PIDD), including the humoral immune defects in common variable immunodeficiency, x-linked agammaglobulinemia, severe combined immunodeficiency and Wiskott-Aldrich syndrome.

IMPORTANT SAFETY INFORMATION

Thrombosis may occur with immune globulin products, including Flebogamma 5% DIF. Risk factors may include: advanced age, prolonged immobilization, hypercoagulable conditions, history of venous or arterial thrombosis, use of estrogens, indwelling central vascular catheters, hyperviscosity, and

[1] Post-polio syndrome - Symptoms - NHS

[2] Wolbert JG, Rajnik M, Swinkels HM, et al. Poliomyelitis. [Updated 2024 Oct 6]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK558944/

[3] Ibid.

[4] Li Hi Shing S, Chipika RH, Finegan E, Murray D, Hardiman O and Bede P (2019) Post-polio Syndrome: More Than Just a Lower Motor Neuron Disease. Front. Neurol. 10:773. doi: 10.3389/fneur.2019.00773

cardiovascular risk factors. Thrombosis may occur in the absence of known risk factors. For patients at risk of thrombosis, administer Flebogamma 5% DIF at the minimum dose and infusion rate practicable. Ensure adequate hydration in patients before administration. Monitor for signs and symptoms of thrombosis and assess blood viscosity in patients at risk for hyperviscosity.

Renal dysfunction, acute renal failure, osmotic nephrosis, and death have been related to intravenous immune globulin (IVIG) products. Patients predisposed to acute renal failure include patients with any degree of preexisting renal insufficiency, diabetes mellitus, age greater than 65, volume depletion, sepsis, paraproteinemia, or patients receiving known nephrotoxic drugs. Administer Flebogamma 5% DIF at the minimum rate of infusion practicable in patients at risk for renal dysfunction or failure. Reports of renal dysfunction and acute renal failure occur more commonly in patients receiving IVIG products containing sucrose as a stabilizer. They account for a disproportionate share of the total number of reported cases of renal dysfunction and acute renal failure. Flebogamma 5% DIF does not contain sucrose.

Flebogamma 5% DIF is contraindicated in patients who have had a history of anaphylactic or severe systemic hypersensitivity reactions to the administration of human immune globulin and in IgA-deficient patients with antibodies to IgA and a history of hypersensitivity.

Severe hypersensitivity reactions may occur with IVIG products, including Flebogamma 5% DIF. In case of hypersensitivity, discontinue Flebogamma 5% DIF infusion immediately and institute appropriate treatment.
Monitor renal function, including blood urea nitrogen (BUN), serum creatinine, and urine output in patients at risk of developing acute renal failure.

Hyperproteinemia, increased serum viscosity, and hyponatremia may occur in patients receiving Flebogamma 5% DIF therapy.

Aseptic meningitis syndrome (AMS) has been reported to occur following IVIG treatment. AMS may occur more frequently following high dose (eg, > 1.0 g/kg body weight) and/or rapid infusion of IVIG.

Hemolysis, either intravascular or due to enhanced red blood cell sequestration, can develop subsequent to Flebogamma 5% DIF treatments. Risk factors include high doses and non-O blood group. Monitor patients for hemolysis and hemolytic anemia.

Noncardiogenic pulmonary edema (transfusion-related acute lung injury [TRALI]) has been reported in patients following IVIG treatment. If TRALI is suspected, perform appropriate tests for the presence of antineutrophil antibodies and anti-HLA antibodies in both the product and patient serum.

Individuals receiving Flebogamma 5% DIF for the first time or being restarted on the product after a treatment hiatus of more than 8 weeks may be at a higher risk for the development of fever, chills, nausea, and vomiting. Careful monitoring of recipients and adherence to recommendations regarding dosage and administration may reduce the risk of these types of events.

Because Flebogamma 5% DIF is made from human plasma, it may carry a risk of transmitting infectious agents, eg, viruses, the variant Creutzfeldt-Jakob disease (vCJD) agent, and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent. This also applies to unknown or emerging viruses and other pathogens. No cases of transmission of viral diseases or CJD have been associated with the use of Flebogamma 5% DIF.

Periodic monitoring of renal function and urine output is particularly important in patients judged to be at increased risk of developing acute renal failure. Assess renal function, including measurement of BUN and serum creatinine, before the initial infusion of Flebogamma 5% DIF and at appropriate intervals thereafter.
Consider baseline assessment of blood viscosity in patients at risk for hyperviscosity, including those with cryoglobulins, fasting chylomicronemia/markedly high triacylglycerols (triglycerides), or monoclonal gammopathies, because of the potentially increased risk of thrombosis.

After infusion of IgG, the transitory rise of the various passively transferred antibodies in the patient's blood may yield positive serological testing results, with the potential for misleading interpretation.

Flebogamma 5% DIF contains sorbitol. The presence of sorbitol presents a risk to those with hereditary fructose intolerance (HFI). Flebogamma 5% DIF must not be administered to subjects with HFI.

The most common adverse reactions (reported in at least 5% of clinical trial adult subjects) were headache, pyrexia/fever, pain, infusion site reactions, diarrhea, rigors or chills, urticaria, and infusion site inflammation.

The most common adverse reactions (reported in at least 5% of clinical trial pediatric subjects) were headache, pyrexia, hypotension, tachycardia, diastolic hypotension, nausea, abdominal pain, diarrhea, pain, and vomiting.

For more information, please check the U.S. prescribing information here.

Always refer to the local prescribing information approved in your country.

About Grifols

Grifols is a global healthcare company founded in Barcelona in 1909 committed to improving the health and well-being of people around the world. A leader in essential plasma-derived medicines and transfusion medicine, the company develops, produces and provides innovative healthcare services and solutions in more than 110 countries.

Patient needs and Grifols' ever-growing knowledge of many chronic, rare and prevalent conditions, at times life-threatening, drive the company's innovation in both plasma and other biopharmaceuticals to enhance quality of life. Grifols is focused on treating conditions across four main therapeutic areas: immunology, infectious diseases, pulmonology and critical care.

A pioneer in the plasma industry, Grifols continues to grow its network of donation centers, the world's largest with close to 400 across North America, Europe, Africa and the Middle East, and China.

As a recognized leader in transfusion medicine, Grifols offers a comprehensive portfolio of solutions designed to enhance safety from donation to transfusion, in addition to clinical diagnostic technologies. It provides high-quality biological supplies for life-science research, clinical trials and for manufacturing pharmaceutical and diagnostic products. The company also supplies tools, information and services that enable hospitals, pharmacies and healthcare professionals to efficiently deliver expert medical care.

Grifols, with more than 23,800 employees in more than 30 countries and regions, is committed to a sustainable business model that sets the standard for continuous innovation, quality, safety and ethical leadership.

The company's class A shares are listed on the Spanish Stock Exchange, where they are part of the IBEX-35 (MCE:GRF). Grifols non- voting class B shares are listed on the Mercado Continuo (MCE:GRF.P) and on the U.S. NASDAQ through ADRs (NASDAQ:GRFS).

For more information about Grifols, please visit www.grifols.com

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