**AN INTERNATIONAL, MULTICENTRE, EFFICACY AND SAFETY STUDY OF I10E/ IQYMUNE IN INITIAL AND MAINTENANCE TREATMENT OF PATIENTS WITH CHRONIC INFLAMMATORY DEMYELINATING POLYRADICULONEUROPATHY (CIDP) - PRISM STUDY**

Eduardo NOBILE-ORAZIO for PRISM study investigators(1), Richard HUGHES(2), Isabel ILLA(3), Jean-Marc LÉGER(4), S.J. Ingemar MERKIES(5), Lucas PADUA(6), Witold MALYSZCZAK(7), Sophie PUGET(8)

**INTRODUCTION**

The EFNS/PNS guideline 2010(1) recommends the use of IVIg (level A recommendation) or corticosteroids (level C recommendation) as a first-line treatment in CIDP. For the maintenance treatment, if IVIg is effective in first-line, it can be continued until the maximum benefit has been achieved then the dose should be the lowest effective maintenance dose. LFB BIOTECHNOLOGIES is currently conducting a clinical trial in CIDP with their new 10% liquid IVIg (I10E).

**KEY POINTS**

1. This study is a phase III, international, multicentre, prospective clinical trial (NTC 02934460).
2. The objective of this study is to provide confirmatory data on the efficacy and safety of I10E in the initial and maintenance treatment of CIDP over 21 weeks. An extension study (PRISM-2) is also planned for accessing the efficacy of I10E administered at a reduced maintenance dose in sustaining CIDP response after an initial 6-month treatment.

**METHODS**

This study is an international, multicentre, efficacy and safety study of I10E/ IQYMUNE in initial and maintenance treatment of patients with CIDP. Inclusion criteria are defined as patients with a decrease ≥ 1 point in the adjusted INCAT disability score between baseline and EOS visit.

**ENDPOINTS**

- **EFFICACY ENDPOINTS**
  - **PRIMARY:**
    - Responder rate at End of Study (EOS) visit (responders are defined as patients with a decrease ≥ 1 point in the adjusted INCAT disability score between baseline and EOS visit).
  - **SECONDARY:**
    - Percentage of patients at 12 weeks and EOS visit with no change in CIDP treatment
    - Grip strength with the Martin dynamometer in both hands
    - Rasch-built Overall Disability Scale (R-ODS)
    - Patient and Investigator Clinical Global Impression (CGI)
    - MRC 12 muscles sum score (0 to 5) and Rasch-modified MRC (0 to 3)

- **EXPLORATORY ENDPOINTS**
  - B cell activating factor (BAFF) and complement components (C3 and C4 antigens, CH50)
  - Serum total IgG functions preserved
  - Anti-contactin 1 and anti-neurofascin 155 antibodies titers
  - FcγRIIB B cells marker levels
  - Change from baseline to EOS visit nerve conduction velocities, distal latency, amplitude of the negative phase of compound muscle action potentials and F wave latency for the following peripheral nerves: median nerve, ulnar nerve and peroneal nerve
  - Change from baseline to EOS visit nerve maximal/minimal cross section area, intra-nerve and inter-nerve variability

**INCLUSION CRITERIA (PRISM STUDY)**

- Male or female aged 18 years or more
- Definite or probable CIDP according to the EFNS/PNS guideline 2010 and neurophysiological criteria
- Pure motor CIDP, provided that a diagnosis of MMN has been ruled out.
- CIDP associated with monoclonal gammopathy of undetermined significance (MGUS) provided that anti-MAG antibodies titer is lower than the used technique's negativity threshold (1000 BTU)
- Lewis-Summer syndrome
- Score of at least 2 on the adjusted INCAT disability scale
- Patient who either:
  - Has never been previously treated with IVIg
  - Or was previously treated with IVIg but is in clinical relapse following treatment withdrawal
- Covered by national health care insurance system if required by local regulations
- Written informed consent obtained prior to any study-related procedures

**CONCLUSIONS**

These prospective open label studies (PRISM and PRISM-2) are planned to assess the efficacy and safety of I10E in the initial and maintenance treatment (during 18 months) in patients with CIDP. These studies will also evaluate the role of different scales in the assessment of clinical response.

**BIOMARKER STUDY:**

- Change from baseline to EOS visit nerve conduction velocities, distal latency, amplitude of the negative phase of compound muscle action potentials and F wave latency for the following peripheral nerves: median nerve, ulnar nerve and peroneal nerve
- Change from baseline to EOS visit nerve maximal/minimal cross section area, intra-nerve and inter-nerve variability
- US immune-related classification (electrophysiology examination and peripheral nerve ultrasonography) in the following peripheral nerves: median nerve, ulnar nerve, peroneal nerve and sural nerve

**SAFETY ENDPOINTS**

- Treatment-emergent adverse events including Serious Adverse events
- Adverse events temporally associated to infusion i.e., that begin during an infusion or within 72 hours after an infusion.
- Clinically significant changes from baseline in vital signs and laboratory tests

**UPDATE**

- 42 patients are expected:
  - 21 lg-naive patients
  - 7 countries
  - 37 sites

**REFERENCES**

(1) Humanitas Clinical and Research Center, Milan University, Milan, Italy; (2) MRC Centre for Neuromuscular Disease, National Hospital for Neurology and Neurosurgery, London, England; (3) Hospital Sant Pau, Universitat Autònoma Barcelona, Spain; (4) University Hospital Pitié-Salpêtrière, Paris, France; (5) Rheumatology University Medical Center – Pirmasens & Speyer Hospital, Pirmasens, Germany; (6) UCB Biopharma Spain S.L.; (7) Clinical Research and Development, LFB BIOTECHNOLOGIES, Les Ulis, France; (8) International Scientific Affairs unit, LFB BIOMEDICAMENTS, Les Ulis, France