IRLAB provides in-depth information on results from successful Phase IIa study with IRL752 in Parkinson's disease

The explorative analysis of efficacy data from the Phase IIa study with IRL752 indicates that the substance has potential to improve symptoms of Parkinson's disease strongly linked to the brain's executive functions, which today lack effective treatment. IRLAB is therefore planning to carry out an efficacy study (Phase IIb) focusing on executive functions – axial motor symptoms and cognitive symptoms in patients with Parkinson's disease and dementia.

The phase IIa study's primary endpoint was safety and tolerability of the drug candidate. IRLAB has previously reported that IRL752 was well tolerated by patients. Additional efficacy measurements were performed with standardized and internationally recognized scales for motor and mental functions, as well as cognitive tests. In the explorative analysis of effect, symptoms that are strongly linked to the brain's so-called executive functions improved in the patient group treated with IRL752 but not in the placebo group, as described in more detail below.

"Leading international experts, KOLs, believe that it is very important to develop treatments against impaired executive functions with axial motor symptoms and dementia, thus strongly supporting IRLAB's development strategy for IRL752. The study results are also in line with the results of previous preclinical studies and once again demonstrate the value in our research platform, ISP's, ability to detect new potential treatments", said Dr. Nicholas Waters, IRLAB CEO.

Impaired executive functions in Parkinson's disease are associated with cognitive impairment, axial motor symptoms and a general lack of ability for initiative and activity. Through the amplification of signal transmission between nerve cells in parts of the brain that are linked to executive functions, IRL752 has potential to treat symptoms of Parkinson's disease, which today lack effective treatment.

"The explorative analysis of the study indicates effects of IRL752 on symptoms that are very difficult to treat with presently available drugs. The effect on executive symptoms, which goes beyond the symptoms responding to levodopa treatment, supports the hypothesis that IRL752 affects the systems in the brain that hitherto has been difficult to treat. The results create favorable conditions for the design of the forthcoming Phase IIb effect study with IRL752", said Dr. Joakim Tedroff, IRLAB's Chief Medical Officer.

Axial motor functions

In the explorative analysis of the effect on axial motor symptoms in the patient group treated with IRL752, the sum of the scores of speech, swallowing, falling (unrelated to freezing) and freezing when walking improved (reduced) by 12% (p=0.029) from study day 1 to 28 (sum of UPDRS part 2 item 5, 7, 13 and 14). In the placebo group, the corresponding change was 0% (p=1,000).

The sum of the scores of falling (unrelated to freezing) and freezing when walking was improved by 29% (p=0.002) from study day 1 to 28 (sum of UPDRS part 2, item 13 and 14). In the placebo group, the corresponding change was 0% (p=1.000). The results are supported by improvement in a balance test, retropulsion pull test, (UPDRS part 3, item 30. p=0.043). In placebo-treated patients no change was seen.

Cognitive and neuropsychiatric tests

Furthermore, a non-significant trend towards improved results in more complex cognitive tests conducted in the study was recognized. These tests were performed with a validated online test tool (Cambridge Cognition Ltd, UK). In the most complex test, OTS (One touch stocking of Cambridge), patients in the IRL752 treatment group solved tasks in their first attempt more often (OTS first choice accuracy, +43%) and the tests were performed somewhat faster (OTS median latency, -6.5%) after four weeks of treatment. In the placebo group, the corresponding result for OTS-first choice accuracy was + 25%, OTS median latency was -1%,

In the group treated with IRL752, a 75% decrease in apathy/indifference was observed (p=0.004), estimated by the NPI-12 scale (Neuropsychiatric inventory-12). This observation was supported by a reduction of reported caregiver distress by 75% (p=0.029). In the group treated with placebo, the measures of apathy/indifference (decrease by 33%) and caregiver distress (decrease by 25%) were not significant.

Other analyses

After individual dose titration, day 1-14, the mean dose day 15-28 in the study was 600 mg/day in the IRL752 group and 775 mg/day in the placebo group.

In the study, the group treated with IRL752 had a numerical decrease in Parkinson's symptoms, as measured by UPDRS. In UPDRS Part 1, the score fell by 10%, in UPDRS Part 4 by 17% and in UPDRS Part 4 item 36-39 (measurements of "off" symptoms) by 25% after 28 days of treatment. These numerical changes were not significant. For the placebo group, the corresponding changes were 0%, 0% and 0%.

Treatment with IRL752 or placebo did not affect results in the Freezing of gait questionnaire (FOGQ) or Timed up and go test (TUG) or in appendicular symptoms in the UPDRS.

In patients treated with IRL752, adverse events were mainly related to the central nervous system (CNS), gastrointestinal systems and infections. These were of mild to moderate intensity and occurred predominantly during the initial 14 day titration phase when 68% of patients treated with IRL752 reported adverse reactions. After determination of individual treatment doses, days 15-28, 11% of patients reported adverse reactions. In the IRL752 treated group a moderate increase in liver enzymes was seen in three patients at end of treatment which recovered at follow-up. Corresponding side effect frequency in the placebo group show that 14% reported adverse events during the first 14 days and 29% during day 15-28.

The full results of the study will be published in an international scientific journal.

About the study

The study, IRL752C002 (EudraCT # 2017-001673-17), was intended to investigate the safety and tolerability of the drug candidate. In the study, patients were given active substance or placebo for four weeks. Additional estimates were made with standardized and internationally recognized scales for motor and mental functions, as well as cognitive tests adapted for Parkinson's disease. The design of the study does not allow conclusive conclusions to be drawn about the effect.

The study was randomized, double-blind, placebo controlled and run at 9 centres in Sweden and one in Finland. Forty-three (43) patients with advanced Parkinson's disease and dementia were screened for participation in the study and 32 were randomized to four weeks of treatment, 25 with IRL752 and 7 with placebo. In the IRL752 treated group 23 of 25 patients completed the entire treatment period and 6 of 7 in the placebo group.

Placebo or IRL752 (300-750 mg/day) was titrated during two weeks followed by stable dosing for the remaining two weeks. Tolerability and safety were continuously monitored. Mean age was 72 years, 28 patients were male and 4 female. All patients had advanced stage Parkinson's disease, 18 in Hoehn and Yahr stage 3-4. The average minimal mental state examination (MMSE) was 22.6 points on entry to the study.

About Unified Parkinson's Disease Rating Scale (UPDRS)

Unified Parkinson's Disease Rating Scale (UPDRS) is a standardized and validated estimation scale developed for people with Parkinson's disease (Movement Disorder Society Task Force on Rating Scales for Parkinson's Disease, 2003). The instrument has been tested for good reliability and validity.

The instrument consists of four parts.

Part I - Mentation, Behavior and Mood

Part II - Activities of Daily Living

Part III - Motor Examination

Part IV - Complications of therapy

Each section has questions that rate the symptoms from 0 to 4 where higher values indicate more severe symptoms.

IRL752

IRL752 is developed for the treatment of Parkinson Disease Dementia (PD-D) ultimately affecting up to 80 % of all PD patients. Effective treatments are lacking and thus, the medical need is huge. IRL752 has the ability to increase synaptic availability of the neurotransmitters norepinephrine and dopamine in the frontal cortex and also activates expression of genes modulating synaptic activity and plasticity. Clinical research has shown that both norepinephrine and dopamine neurotransmitters are reduced in frontal cortical brain areas in PD-D. By counteracting this reduction, treatment with IRL752 may improve cognitive and psychiatric symptoms in these patients.

IRL752 primary targets are brain 5HT7 and cortical Alpha receptors as an antagonist leading to improvement of disturbed cognitive function, antidepressant and antipsychotic effects. These are all desired properties for the treatment of PD-D.

For further information

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About IRLAB

IRLAB is a research and development company, listed on Nasdaq First North Premier, focused on development of novel therapies for the treatment of neurodegenerative diseases, in particular Parkinson's disease.

IRLAB has two clinical candidate drugs, IRL752 and IRL790, focused on medical needs in Parkinson's disease. IRLAB also has additional programs in pre-clinical stages.

IRLAB's research is aimed at discovery and development of new candidate drugs addressing unmet medical need in diseases of the central nervous system, using the unique and proprietary integrative screening process, ISP.

IRLAB is based in Gothenburg, Sweden. The operations are mainly carried out through the subsidiary Integrative Research Laboratories Sweden AB.

For more information, please visit www.irlab.se.