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Company:	CYBERDYNE Inc.
Name of Representative:	Yoshiyuki Sankai, President and CEO
Code:	7779 (Mothers Section of the Tokyo Stock Exchange)
Contact:	Shinji Uga, Director and CFO (Tel. +81-29-869-9981)

【News】Details report of the investigator-initiated clinical trial of Medical HAL for neuromuscular disease patients published in an international medical journal

CYBERDYNE Inc. (Tsukuba, Ibaraki, Japan; President and CEO: Yoshiyuki Sankai; from now on referred to as "the Company") announced that the results of the investigator-initiated clinical trial of the Medical HAL for patients with neuromuscular diseases are now available on an international medical journal. The paper titled "Cybernic treatment with wearable cyborg Hybrid Assistive Limb (HAL) improves ambulatory function in patients with slowly progressive rare neuromuscular diseases: a multicentre, randomised, controlled crossover trial for efficacy and safety (NCY-3001)" was written by Dr. Takashi Nakajima (Director, Niigata Hospital, National Hospital Organization), the study coordinator. The journal was included in the international medical journal "Orphanet Journal of Rare Diseases" in July 2021. The journal is the result of a multicenter clinical trial consisting of teams from National Hospital Organization Niigata National Hospital, National Hospital Organization Tokushima National Hospital, National Center of Neurology and Psychiatry, Jichi Medical University, Kyoto Prefectural University of Medicine, National Hospital Organization Osaka Toneyama Medical Center, Tokyo Women's Medical University, National Hospital Organization Iou National Hospital, and Tsukuba University Faculty of Medicine.

We will continue to utilize this paper as compelling evidence for global standard treatment in procedures such as insurance listing in various countries.

URL link to the paper
https://ojrd.biomedcentral.com/articles/10.1186/s13023-021-01928-9

About the outline of the paper

To evaluate the efficacy and safety of HAL, a randomized, controlled, crossover study took place at nine centers in patients with neuromuscular diseases (*1) aged 18 years or older who were unable to walk 10 m without assistance or support. The primary endpoint was a 2-minute walking distance, and secondary endpoints included 10-m walking speed, manual muscle testing (MMT), and multiple functional assessments. The trial also evaluated adverse events, failures, and errors.

Thirty patients were randomly assigned to two groups (Group A and Group B) (13 patients in Group A and 11 patients in Group B were included in the final analysis), and Cybernic Treatment (using HAL and hoist) and control treatment (using hoist) were performed in a crossover fashion. After comparing the results of nine sessions of 40-minute walking programs (*2), the efficacy of the group who went through Cybernic Treatment improved by 10.066% compared to the control treatment in the primary endpoint of 2-minute walking distance, which was statistically significant (95% confidence interval 0.667 – 19.464; p=0.0369). In addition, the secondary endpoints showed significant improvement in MMT total score and cadence (walking rate) during the 10-meter walk test. The only adverse events were mild to moderate myalgia, back pain, and skin problems at the contact area, which healed easily.

In conclusion, for patients with intractable and progressive neuromuscular diseases, treatment with HAL, a new therapeutic device, proved to be more effective and safer than conventional treatment.

(*1)Neuromuscular Diseases: spinal muscular atrophy (SMA), spinal and bulbar muscular atrophy (SBMA), amyotrophic lateral sclerosis (ALS), Charcot-Marie-Tooth disease, distal myopathy, inclusion body myositis, congenital myopathy, and muscular dystrophy.
(*2) In the results of post-marketing surveillance of the medical HAL Lower Limb Type conducted after this clinical trial, even better improvement was shown by providing additional courses of treatment with some time interval (each course consisting of 9 treatment sessions). Moreover, with the additional courses of treatment, even after 3.5 years, the walking function of patients with neuromuscular diseases could still walk at a level higher than that before the start of treatment.

＜What is the significance of this paper?
This paper officially announces the detailed results of the investigator-initiated clinical trial (NCY-3001 study) conducted from March 2013 to August 2014. Using the results of the said clinical trial, the Company has achieved significant milestones so far.

- Obtained manufacturing and marketing approval as a new medical device in Japan in November 2015
- Obtained medical insurance listing under a new category in Japan April 2016
- Expansion of indications for MDD certification in Europe May 2016
- Expansion of indications for 510k clearance in the U.S. October 2020

In addition, data supporting the results of this paper were obtained in the results of post-marketing surveillance of HAL for Medical Use Lower Limb Type from November 26, 2015, to November 25, 2020. Results of post-marketing surveillance show that the clinical trials described in this paper were conducted with a high degree of accuracy, assuming actual clinical use.

The Company will utilize the published paper to accelerate the installation of Medical HAL in each region and for various procedures such as insurance coverage while making further efforts to establish Cybernics Treatment with HAL as a global standard for intractable neuromuscular diseases.

＜(Comment by Dr. Takashi Nakajima, President of National Hospital Organization Niigata Hospital)
The process of randomized controlled trials for the application of medical device approval is called a clinical trial, and it is the most important scientific method for evaluating new medical devices. This clinical trial verified the groundbreaking efficacy and safety of a medical device for progressive intractable neuromuscular disease (*1), for which methods that induce functional recovery did not exist before. This trial pioneered a new medical concept of neuroplasticity and functional regeneration, which was why it took a long time to write and review the academic paper. Now that the report has been rigorously reviewed and accepted by a leading international journal, the treatment method with HAL is now fully documented. Since the trial proved the performance of HAL in the medical field, which is said to be the most difficult to develop treatment method, it will change the treatment method at the level of international medical societies. The result shall accelerate the initiatives of CYBERDYNE to disseminate HAL as a standardized method of treatment. In addition, this trial proved a groundbreaking research result for a new approach to the combined therapy of HAL and advanced drugs, which is currently attracting attention.

The following grants were used for the planning and implementation of this clinical trial.

- Research to overcome intractable diseases (Ministry of Health, Labour and Welfare, Grant-in-Aid for Scientific Research 2012 – 2014)
  Research on physician-initiated clinical trials for a new medical device, a lower limb wearable assistive robot (HAL-HN01) with voluntary control by bioelectricity, etc., to achieve therapeutic effects in inhibiting the progression of rare intractable diseases
- Research for practical application of intractable diseases (AMED 2015 – 2017)
  Multicenter physician-initiated clinical trials for the practical application of a new treatment for walking disability in rare intractable brain and spinal cord diseases using a biopotential-driven lower limb assistive robot (HAL-HN01)