WORLDWIDE CLINICAL TRIALS | geneuro

CASE STUDY:
MANAGING MULTIPLE OUTCOME MEASURES AND RAPID PATIENT RECRUITMENT FOR PHASE IIB CLINICAL TRIAL ON TARGETING RELAPSE-REMITTING MULTIPLE SCLEROSIS

GENEURO AND WORLDWIDE CLINICAL TRIALS: A MULTIPLE SCLEROSIS CLINICAL TRIAL COLLABORATION

GeNeuro and Worldwide Clinical Trials collaborated on the development of a new, exciting molecule for the treatment of multiple sclerosis (MS). GeNeuro was founded in 2006 to work on endogenous retroviruses, with the mission of developing new drugs and treating patients with neurodegenerative and autoimmune disorders by neutralizing these causal factors. The company's lead product is a monoclonal antibody targeting the protein pHERV-W Env of endogenous retroviral origin.

STUDY FACTS

Phase IIb, double-blind, randomized placebo-controlled study of the investigational product (IP): GNbAC1

Study conducted in:

12 countries

57 sites

270 randomized patients

- **Gender:** mostly females
- **Age:** mid-30s
- Diagnosed with relapse-remitting MS (RRMS)

Patients were randomized into four parallel groups:

A placebo arm and three groups with active GNbAC1 dosed at:

Two pre-planned study periods

- **Period 1:** week 0 to week 24, in which the three active dose groups would be compared directly to placebo.
- **Period 2:** week 25 to week 48, in which placebo patients were re-randomized to one of the 3 doses of active GNbAC1. For Period 2, patients, investigators, and the MRI reading center all remained blinded to the original or re-randomized treatment assignment.

Worldwide Clinical Trials provided full service for this study

HELPING GENEURO WITH ITS STUDY CHALLENGES

THE STUDY NEEDED TO ADDRESS 3 MAIN CHALLENGES.

MANAGEMENT OF MULTIPLE OUTCOME MEASURES: MRI, EDSS, MSFC, PASAT, 9-HPT, T25-FW. Some of these contained limitations. (MRI analysis limited to lesions ≥ 3 mm in diameter, some scanner types incapable of providing reliable MTR data, etc.) How would the study manage multiple outcome measures?

PATIENT RECRUITMENT AND RETENTION: The ability to rapidly and efficiently recruit patients for a placebo-controlled study of relapsing-remitting MS was limited due to the wide availability of marketed products. How would the study handle this challenge?

METHODOLOGY FOR ANALYSIS SETS: There were several different ways to calculate comparative analyses. Which one would produce the highest quality data?

"In implementing the international, Ph2b GNC-003 (CHANGE-MS) study, GeNeuro, along with our co-development partner, Servier, chose Worldwide Clinical Trials as our CRO partner for several reasons, not the least of which was their global reach. Working as partners, we exceeded expectations in the time needed to fully recruit the patient cohort for the study, with Last Patient First Visit achieved a full 5 months ahead of planned. Once both Week 24 and Week 48 Database Locks were complete, we collaborated with Worldwide on a strategy for managing multiple outcome measures and complex comparative data analyses. Overall, the collaboration helped to enable us to discover a potential novel treatment for patients with MS."

— GeNeuro & Servier

WORLDWIDE DELIVERED 3 UNCOMMON SOLUTIONS

MANAGEMENT OF MULTIPLE OUTCOME MEASURES: COORDINATING MULTIPLE VENDORS AND IMPLEMENTING A FLEXIBLE MONITORING APPROACH

The main outcome measures for this study included neuroinflammatory MRI outcomes (T1 Gd+ lesions and T2 lesions); neurodegenerative MRI outcomes (T1 hypointense lesion, brain volumes, and magnetization transfer ration); clinical measures of disease activity and disability-related outcomes; and pharmacokinetic measures. Selected sites had MRI facilities in close proximity, providing easy access for clinical trial patients. Appropriate MRI fees were instituted to ensure the proper performance of the imaging sites. In addition, the monitoring visits for high-enrolling sites were more frequent, and close communication was maintained with medical monitors.

PATIENT RECRUITMENT AND RETENTION: ENROLLMENT SITE AND RETENTION STRATEGY ACHIEVED 87.4% PATIENT RETENTION

Regions with a large number of treatment-naïve subjects were identified, and sites were strategically selected based on their KOLs and track record of good quality to enhance the recruitment rate. Because the ability to maintain patients on placebo in relapsing-remitting MS is limited, the placebo-control period (Period 1 from weeks 0 to 24) was a key limitation. To resolve this challenge, all placebo patients at week 24 were re-randomized to active IP either 6 mg/kg, 12 mg/kg, or 18 mg/kg. But Period 2 was considered to be dose blinded, that is to say patients, investigators, study site staff, and Worldwide Clinical Trials' staff all remained blinded to the original randomization groups and re-randomization groups.

METHODOLOGY FOR ANALYSIS SETS ENABLES EFFICIENCY

The original randomization groups for Period 1 were kept for the analysis covering Periods 1 + 2, hence the comparator group was the originally randomized placebo arm, even though they received active treatment in Period 2, which provided the benefit of maintaining the original randomization scheme. This is a conservative way of analyzing efficacy.

STUDY RESULTS AND OUTCOMES

Q: INVESTIGATORS WERE ASKED:

In comparison with baseline status and the change status (basically, double-blind placebo-control study), what percentage of your patients showed clear improvement or stabilization in clinical status? What percentage of patients showed deteriorated status?

A: INVESTIGATORS REVEALED:

24.3% of patients are feeling better and have a better neurological status than they had at the beginning of clinical study change

62% of patients are at the same stage, which is stabilization

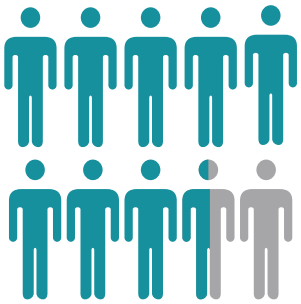
13% of patients showed deterioration of their neurological status

Q: INVESTIGATORS WERE ASKED:

What is the percentage of your patients with a medical rationale to continue current treatment?

A: INVESTIGATORS REVEALED:

87% of patients examined had indication to further treatment with the new molecule



THERE'S NO SUBSTITUTE FOR EXPERTISE
MEET YOUR PARTNERS

Ready to talk trials with a member of the Worldwide Clinical Trials team?

CONNECT WITH OUR MULTIPLE SCLEROSIS EXPERTS

ASK ME A QUESTION

TAMARA AST, PH.D.

Senior Vice President, Therapeutic Area Lead, Neuroscience Global Project Management

Dr. Ast has 23 years industry experience across a variety of neuroscience indications. She has held leadership roles for Project Management and Operations delivery at Worldwide Clinical Trials for the past six years, and now leads the Neuroscience therapeutic area. This business unit includes Worldwide's most experienced Neuroscience clinical research professionals for neurological, psychiatric and pain indications to ensure that the Worldwide team provides sponsors with the best possible regulatory and scientific, medical and operational strategy and clinical trial execution. Dr. Ast has an affinity for dealing with various cultures and working environments, responding quickly to any challenges encountered. She is experienced in managing large multi-cultural teams across different countries and continents, ranging from FIH studies in patients to phase IIIb global trials. Dr. Ast's primary therapeutic and operational expertise has had a specific emphasis on neurological conditions such as Multiple Sclerosis, Alzheimer's disease, Parkinson's disease, pain, and psychiatric indications such as schizophrenia, mood disorders, and substance use disorders. Dr. Ast obtained her Ph.D. in medicinal biochemistry from University of London, United Kingdom.

ASK ME A QUESTION

TOMISLAV BABIC, M.D., PH.D.

Vice President, Neuroscience Franchise

Tomislav Babic is the Vice President of Neuroscience Franchise at Worldwide Clinical Trials, where his responsibilities include aspects of hypothesis generation and testing, protocol/strategic program design and development, as well as analysis and clinical interpretation of results for all phases of clinical development. Throughout his career, Dr. Babic has designed program development plans in advanced Parkinson's disease, multiple sclerosis, Alzheimer's disease, and provided consultancy services. He has had experience as a Therapeutic Area Leader and Principal Investigator in more than 110 Phase II and III clinical trials. Dr. Babic is a board-certified neurologist with a master's degree in clinical pharmacology. He serves as an affiliate Professor of Clinical Neurology and Clinical Research at the Medical University of Zagreb, Croatia, and is the author of more than 70 peer reviewed articles and books in neurodegenerative disorders.

ASK ME A QUESTION

ANNECLAUDE MURATET, PHARMD

Executive Director, Global Project Management, Neuroscience, Neurology Franchise Lead

Dr. AnneClaude Muratet has more than 20 years of clinical research experience at both CRO and pharmaceutical companies. During the past 15 years, her focus was centered around oversight strategy and management of global programs, line management, and business development activities. Dr. Muratet's experience includes a variety of indications in psychiatry and neurology (multiple sclerosis, acute ischemic stroke, agitation in Alzheimer's disease patients, epilepsy, schizophrenia, major depressive disorder, generalized anxiety disorder, sleep, and neuropathic pain) as well as several other indications in rare diseases, spanning the full spectrum of activities and services in Phase I to Phase IV studies and programs.