



MASITINIB SHOWS PROMISING NEUROPROTECTIVE EFFECTS IN NEUROIMMUNE-DRIVEN NEURODEGENERATIVE DISEASE MODEL

A NEW PUBLICATION IN THE SCIENTIFIC JOURNAL *PLOS ONE*, SHOWS THAT MASITINIB CAN LOWER SERUM NEUROFILAMENT LIGHT CHAIN, AN IMPORTANT BIOMARKER FOR NEURODEGENERATIVE DISORDERS, INCLUDING MULTIPLE SCLEROSIS, AMYOTROPHIC LATERAL SCLEROSIS AND ALZHEIMER'S DISEASE

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AB Science SA (Euronext - FR0010557264 - AB) today announced publication of research in the peer-reviewed scientific journal *PLOS One* [1], highlighting the neuroprotective potential of masitinib in a model of neuroimmune-driven neurodegenerative disease. This research demonstrates masitinib's ability to limit neuronal damage, as measured by serum neurofilament light chain (NfL) concentration, and reduce pro-inflammatory cytokine biomarkers, offering hope for its application in treating neurodegenerative diseases.

NfL is a non-specific marker of axonal loss that can serve as a biomarker of a drug's ability to produce a neuroprotective effect. Importantly, neuronal damage, or prevention thereof, can be rapidly assessed by measuring serum NfL concentration in EAE-induced mice. Because EAE is a model of neuroimmune-driven neurodegenerative disease, it is highly relevant to masitinib's mechanism of action in diseases such as progressive multiple sclerosis (MS), amyotrophic lateral sclerosis (ALS), Alzheimer's disease and Parkinson's disease.

The article, entitled *'Tyrosine kinase inhibitor, masitinib, limits neuronal damage, as measured by serum neurofilament light chain concentration in a model of neuroimmune-driven neurodegenerative disease'*, is freely accessible online from the PLOS One website.

Professor Olivier Hermine, MD, President of the Scientific Committee of AB Science and co-author of this article commented: *"This study is the first to demonstrate that masitinib can lower serum NfL levels, a key biomarker of neuronal damage, while also reducing neuroinflammation and slowing functional decline in a neuroimmune-driven disease model. Masitinib has already shown clinical benefits in progressive MS, ALS, and mild-to-moderate AD in previous trials, and this study further strengthens its therapeutic promise. Overall, these findings support masitinib's potential as a disease-modifying therapy for neurodegenerative diseases."*

Masitinib's mechanism of action targets the innate neuroimmune system, specifically mast cells and microglia, which are increasingly recognized as contributors to the pathophysiology of neurodegenerative diseases. These results provide additional evidence regarding the anti neuro-inflammatory properties of masitinib and add further credibility to the masitinib associated neuroprotection observed in late phase clinical trails of progressive multiple sclerosis, amyotrophic lateral sclerosis and Alzheimer's disease.

Key findings include:

- Masitinib significantly reduced serum neurofilament light chain (NfL) levels, indicating its neuroprotective effects in a neuroimmune-driven neurodegenerative disease model.
- Reduction in relative NfL Levels:

- At Day 8, masitinib treatment reduced the relative increase in serum NfL levels as compared with the EAE control group. Specifically:
 - Masitinib 50 mg/kg/day reduced NfL levels by 43%.
 - Masitinib 100 mg/kg/day reduced NfL levels by 60%.
- This reduction was dose-dependent, with the higher dose showing greater efficacy.
- Reduction in absolute NfL Levels:
 - At Day 8, absolute serum NfL concentrations were approximately 25% lower in both masitinib treatment groups as compared with the EAE control group.
 - At Day 15, masitinib further reduced absolute serum NfL levels. Specifically:
 - Masitinib 50 mg/kg/day reduced levels by 6%.
 - Masitinib 100 mg/kg/day reduced levels by 26%.
- Masitinib treatment significantly reduced the levels of several pro-inflammatory cytokine biomarkers in the EAE mouse model, indicating its anti-inflammatory effects.
- Masitinib demonstrated beneficial effects on functional performance in the EAE mouse model, particularly in grip strength:
 - Masitinib-treated mice initially showed deterioration in grip strength but recovered to their pretreatment (Day 1) levels by Day 15.
 - Both masitinib groups (50 mg/kg/day and 100 mg/kg/day) showed significantly less relative deterioration in grip strength at Day 15 compared to the EAE control group ($p < 0.001$).
 - These findings suggest that masitinib slows the deterioration of grip strength, indicating a protective effect on motor function under conditions of chronic neuroinflammation.

Overall, these findings demonstrate that masitinib effectively limits neuronal damage, as reflected by lower serum NfL levels, and supports its potential as a neuroprotective agent in neurodegenerative diseases.

[1] Hermine O, Gros L, Tran T-A, Loussaief L, Flosseau K, Moussy A, Mansfield CD, Vermersch P (2025) PLoS ONE 20(4):e0322199. <https://doi.org/10.1371/journal.pone.0322199>

About the neurofilament light chain (NfL) biomarker

The measurement of neurofilament light chain (NfL) in biological fluids has been proposed for monitoring the therapeutic effect of drugs aimed at reducing axonal damage. NfL are cytoskeletal proteins that are highly specific for neurons in both the central nervous system (CNS) and the peripheral nervous system. NfL in cerebrospinal fluid or the bloodstream is therefore indicative of axonal lesions and/or degeneration and elevated NfL levels are associated with traumatic brain injuries or neurodegenerative diseases (NDD), including amyotrophic lateral sclerosis, multiple sclerosis, and Alzheimer's disease. A growing body of literature shows that because the level of free NfL in serum/plasma directly reflects neuronal damage within the CNS, it can be used as a reliable and easily accessible marker of disease intensity and/or activity across a variety of neurological disorders.

About masitinib

Masitinib is a orally administered tyrosine kinase inhibitor that targets mast cells and macrophages, important cells for immunity, through inhibiting a limited number of kinases. Based on its unique mechanism of action, masitinib can be developed in a large number of conditions in oncology, in inflammatory diseases, and in certain diseases of the central nervous system. In oncology due to its immunotherapy effect, masitinib can have an effect on survival, alone or in combination with chemotherapy. Through its activity on mast cells and microglia and consequently the inhibition of the activation of the inflammatory process, masitinib can have an effect on the symptoms associated with some inflammatory and central nervous system diseases and the degeneration of these diseases.

About AB Science

Founded in 2001, AB Science is a pharmaceutical company specializing in the research, development and commercialization of protein kinase inhibitors (PKIs), a class of targeted proteins whose action are key in signaling pathways within cells. Our programs target only diseases with high unmet medical needs, often lethal with short term survival or rare or refractory to previous line of treatment.

AB Science has developed a proprietary portfolio of molecules and the Company's lead compound, masitinib, has already been registered for veterinary medicine and is developed in human medicine in oncology, neurological diseases, inflammatory diseases and viral diseases. The company is headquartered in Paris, France, and listed on Euronext Paris (ticker: AB).

Further information is available on AB Science's website: www.ab-science.com.

Forward-looking Statements - AB Science

This press release contains forward-looking statements. These statements are not historical facts. These statements include projections and estimates as well as the assumptions on which they are based, statements based on projects, objectives, intentions and expectations regarding financial results, events, operations, future services, product development and their potential or future performance.

These forward-looking statements can often be identified by the words "expect", "anticipate", "believe", "intend", "estimate" or "plan" as well as other similar terms. While AB Science believes these forward-looking statements are reasonable, investors are cautioned that these forward-looking statements are subject to numerous risks and uncertainties that are difficult to predict and generally beyond the control of AB Science and which may imply that results and actual events significantly differ from those expressed, induced or anticipated in the forward-looking information and statements. These risks and uncertainties include the uncertainties related to product development of the Company which may not be successful or to the marketing authorizations granted by competent authorities or, more generally, any factors that may affect marketing capacity of the products developed by AB Science, as well as those developed or identified in the public documents published by AB Science. AB Science disclaims any obligation or undertaking to update the forward-looking information and statements, subject to the applicable regulations, in particular articles 223-1 et seq. of the AMF General Regulations.

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