

Cognitive Vitality Reports® are reports written by neuroscientists at the Alzheimer's Drug Discovery Foundation (ADDF). These scientific reports include analysis of drugs, drugs-in-development, drug targets, supplements, nutraceuticals, food/drink, non-pharmacologic interventions, and risk factors. Neuroscientists evaluate the potential benefit (or harm) for brain health, as well as for age-related health concerns that can affect brain health (e.g., cardiovascular diseases, cancers, diabetes/metabolic syndrome). In addition, these reports include evaluation of safety data, from clinical trials if available, and from preclinical models.

Masitinib

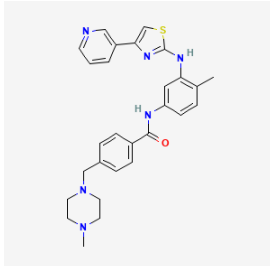
Evidence Summary

Masitinib is a tyrosine kinase inhibitor that has been tested in many conditions, including ALS, MS, and AD, but is not approved for any human indication.

Neuroprotective Benefit: Masitinib has been tested in large clinical trials for AD, ALS, and MS. These trials have reported disease stabilization in some subgroups, but masitinib has not been approved for these indications.

Aging and related health concerns: Masitinib has been tested in different cancer subtypes and for rheumatoid arthritis, severe asthma, and COVID-19. Despite some reports of positive results, development for these indications has not continued.

Safety: Common adverse events of masitinib include rash, gastrointestinal events, abnormal lab values like neutropenia, and edema. Elevated transaminases have been seen. These events are serious and lead to study discontinuation more often than placebo.

Availability: In clinical development for humans.	Dose: Masitinib is taken by mouth. Dosing is still being optimized. Trials in neurodegenerative diseases are testing doses of 3 mg/kg twice per day by mouth as starting doses, with dose escalations up to 4.5 mg/kg twice per day, usually after 4 weeks of treatment.	Chemical formula: C ₂₈ H ₃₀ N ₆ OS MW: 498.6 g/mol 
Half-life: Average half-life is approximately 24 hours	BBB: Penetrant.	
Clinical trials: Average half-life is approximately 24 hours	Observational studies: No observational studies of masitinib were identified.	
		Source: PubChem

What is it?

Mast cells are innate immune cells that reside in tissue. They are found throughout the body and participate in the inflammatory cascade. They are classically associated with allergic reactions and produce range of immune mediators, including histamine, prostaglandins, and cytokines ([Fong & Crane, 2023](#)). c-Kit, also known as CD117 or stem cell factor receptor, is a transmembrane protein that is a member of the type III receptor tyrosine kinase family, and is a marker of mast cells. c-Kit acts as a receptor for stem cell factor (SCF), which is a hematopoietic cytokine. SCF and c-kit signaling play a role in survival, proliferation, and differentiation of hematopoietic cells, including regulation of red blood cell production, proliferation of lymphocytes, and mast cell development and function ([Liang et al., 2013](#)). Over the course of hematopoietic differentiation, c-kit expression is lost by many hematopoietic cell types, but it is retained in mast cells, natural killer cells, and dendritic cells ([Sheikh et al., 2022](#)). SCF is also upregulated in inflammatory conditions and therefore may be a target for diseases with an inflammatory component ([Dubreuil et al., 2009](#)). SCF and c-kit also participate in regulation of melanogenesis and gametogenesis ([Dubreuil et al., 2009](#)) and development of interstitial cells of Cajal that are involved in gut peristalsis. It is hypothesized that SCF and c-kit signaling contribute to stemness in some organs ([Sheikh et al., 2022](#)). Mutations in the gene encoding c-kit that cause constitutive activation of the tyrosine kinase have been associated with various cancers ([Dubreuil et al., 2009](#)).

Masitinib is a tyrosine kinase inhibitor that is best known as an inhibitor of c-kit and can modulate mast cell survival and function. Masitinib also inhibits PDGFR ([Dubreuil et al., 2009](#)), Lyn, and Fyn ([Hermine et al., 2025](#)). Given the role of mast cells in inflammatory cascades and the contribution of inflammation to many diseases, the mast cell modulating properties of masitinib have led to clinical interest. Masitinib has been tested in a range of indications that either involve aberrant c-kit activation, abnormal activity of mast cells, or chronic inflammation, including prostate and pancreatic cancer, severe asthma, and mastocytosis, as well as multiple sclerosis (MS), amyotrophic lateral sclerosis (ALS), and Alzheimer's disease ([AB Science](#)). Masitinib has not been approved for any human indications as of May 2026 but has been approved for use in canine cancers in Europe and the US ([press release](#)).

Neuroprotective Benefit: Masitinib has been tested in large clinical trials for AD, ALS, and MS. These trials have reported disease stabilization in some subgroups, but masitinib has not been approved for these indications.

Types of evidence:

- 1 network meta-analysis
- 5 clinical trials
- 1 professional resource
- 5 reviews
- Numerous laboratory studies

Human research to suggest prevention of dementia, prevention of decline, or improved cognitive function:

No published research has assessed whether masitinib can prevent dementia, decline, or improve cognitive function.

Human research to suggest benefits to patients with dementia:

Masitinib has been tested in clinical trials for three neurodegenerative conditions: Alzheimer's disease, amyotrophic lateral sclerosis (ALS), and multiple sclerosis (MS).

Alzheimer's Disease

[Dubois et al., 2023](#) describes the results from AB09004, a randomized controlled Phase 3 trial of masitinib. The trial enrolled patients with probable AD (biomarker confirmation was not required for inclusion), MMSE scores of 12 to 25, and had been treated with the standard of care of cholinesterase inhibitor and/or memantine for at least 6 months prior to screening. The trial randomized 718 patients to either placebo or masitinib treatment by mouth. The trial had a series of protocol amendments as to the dosing of masitinib, described in more detail in the 'Safety' section. The final analysis had the following dosing groups:

Group	N
4.5 mg/kg per day	370 total (185 masitinib, 185 placebo)
Initial dose 4.5 mg/kg for 12 weeks, titrated to 6 mg/kg per day	278 total (186 masitinib, 96 placebo)
3 mg/kg per day (dosing paradigm terminated early)	58 (58 masitinib)
6 mg/kg per day starting dose (dosing paradigm terminated early)	12 total (7 masitinib vs. 5 placebo)

The statistical analysis for the primary and secondary outcomes treated the trial as two parallel-group trials; the first compared patients who received 4.5 mg/kg per day of masitinib to placebo, and the second compared those who received 4.5 mg/kg per day of masitinib for 12 weeks and then 6 mg/kg masitinib per day for the remainder of trial, compared to placebo.

The primary outcome was the change in cognitive function as measured by ADAS-cog or daily functioning as measured by ADCS-ADL from baseline to the end of the 24-week dosing. At the end of the trial, the 4.5 mg/day masitinib group (n=182) had a significant improvement of cognitive function from baseline compared to the placebo group (n=176) (least-square mean (LSM)=-2.15; 97.5% CI -3.48 to -0.81; p<0.001). The other primary endpoint of daily functioning as measured by the ADCS-ADL was numerically in favor of the masitinib group compared to placebo, though this did not reach statistical significance (LSM=1.82; 97.5% CI -0.15 to 3.79; p=0.038), as their statistical analysis dictated a significance threshold of 0.025 for the two primary endpoints. Patients treated with masitinib had a statistically significant increased probability of cognitive improvement by the end of the trial as measured by clinical responder rate (22.5% vs 13%, respectively; OR=1.96; 95% CI 1.11 to 3.46; p=0.02) as well as a significant benefit on the Clinician's Interview-Based Impression of Change Plus caregiver

input (CIBIC-Plus) (OR=1.71; 95% CI 1.02 to 2.85; $p=0.040$). There was no difference in cognitive function between groups as measured by CDR or MMSE.

There was no significant difference between the placebo and the group titrated to 6 mg/kg masitinib on either ADAS-cog or ADCS-ADL; analyses of secondary endpoints were therefore not performed on this dataset. The researchers hypothesized that the lack of significant effects observed in this group was in part due to a better-than-expected performance of the placebo group. All participants were also on background cholinesterase and/or memantine therapy. It is worth noting though that the higher-dose masitinib group did not show the same improvement that the lower-dose masitinib group showed on either ADAS-cog or ADCS-ADL. The researchers concluded that a dose of 4.5 mg/kg per day is the recommended dose for future clinical development.

The phase 2 results of masitinib in patients with AD were published by [Piette et al., 2011](#). This trial enrolled patients with mild-to-moderate AD (MMSE between 12 and 26, CDR of 1 or 2) who were also treated for at least 6 months with a stable dose of a cholinesterase inhibitor and/or memantine. A total of 34 patients were randomized to receive either 3 mg/kg per day of masitinib ($n=12$), 6 mg/kg per day of masitinib ($n=14$), or placebo ($n=8$). The rate of clinically relevant cognitive decline as defined by an increase of more than 4 points on ADAS-cog was significantly lower in the masitinib group compared to placebo group at 12 and 24 weeks (6% vs. 50% for both time points). The masitinib group showed improvement or stabilization in cognitive function as assessed by ADAS-cog and MMSE, respectively, whereas the placebo group showed decline on both assessments; there was a statistically significant benefit of masitinib compared to placebo on both assessments at both time points. The masitinib treated patients also showed improvements in daily functioning as measured by ADCS-ADL, though this was significantly better than placebo at 12 weeks but not 24.

ALS

One trial investigating the impact of masitinib in patients with ALS has been completed and published in [Mora et al., 2020](#). The 48-week study known as AB10015 randomized 394 patients with ALS to receive placebo, 3 mg/kg masitinib per day, or 4.5 mg/kg masitinib per day. All patients were on concurrent riluzole treatment (100 mg per day). The trial had a blinded transition from phase 2 to phase 2/3. During the trial the researchers also prospectively defined a two-tiered analysis design wherein patients were stratified as 'normal progressors', defined as an ALSFRS-R progression rate of <1.1 per month from disease-onset to baseline assessment or included in the total dataset of normal and fast progressors.

The primary efficacy population was normal progressors receiving 4.5 mg/kg per day; the other groups including the broader population of normal + fast progressors receiving high-dose masitinib, along with the normal progressors receiving low-dose masitinib and the normal + fast progressors receiving low-dose masitinib were secondary efficacy populations. It is estimated that approximately 85% of ALS patients are normal progressors.

The trial achieved its primary endpoint; there was a significant benefit of masitinib over placebo in normal progressors receiving high-dose masitinib compared to placebo on the ALSFRS-R (LSM=3.4; (95% CI 0.65 to 6.13; $p=0.016$), evidenced by a significantly blunted decline in the masitinib group (change of -9.24 on ALSFRS-R) compared to the placebo group (change of -12.64 on ALSFRS-R). This corresponds to a 27% slowing of rate of functional decline. There was no significant difference between the placebo group and high-dose masitinib in the normal + fast progressor overall group; nor was there any significant difference between the placebo group and the low-dose masitinib groups in either the normal progressors or the overall study. Secondary endpoint analyses indicated that normal progressors receiving high dose masitinib had significantly preserved quality of life and respiratory function compared to placebo. The high dose masitinib group also showed significant 25% delay in disease progression compared to placebo, with an average of 20 months to disease progression compared to 16 months for the placebo group ($p=0.016$). However, there was no difference in median overall survival between any of the groups during the RCT stage of the trial. Subgroup analyses suggested that earlier treatment initiation was associated with greater treatment effect on the ALSFRS-R and time-to-progression analysis, in both normal progressors and in the overall normal + fast progressor cohort.

Other publications have included further follow-up or subgroup analysis of AB10015.

[Mora et al., 2021](#) describes a follow-up assessment of the long-term survival of all participants in AB10015. The researchers collected data on the survival status of 96% of all patients who were randomized in the AB10015 trial; the remaining 4% were evenly spread between arms. The original 48-week trial began in April 2013. There was an associated double-blind extension until data readout, and then a post-study unblinded follow-up period from November 2017 until June 2020. The researchers also defined further stratifications of disease severity as defined by a score of at least 2 on each item on the ALSFRS-R and/or progression rate of less than 1.1 on the ALSFRS-R.

With an average of 75 months since diagnosis, there was no overall survival (OS) benefit of the high dose of masitinib over placebo. However, there was a significant 25 month survival benefit ($p=0.037$) in

patients who had less severe disease at baseline (n=50) and received high dose masitinib (median OS=69 months; 95% CI 44 to non-estimable (NE)) compared to patients who have less severe disease at baseline and received placebo (n=63) (median OS=44 months; 95% CI 31 to 62 months). A similar 25-month significant survival benefit was observed in those who had less severe baseline disease and a normal progression rate and received high dose masitinib compared to those with similar disease characteristics, but who received placebo (p=0.025). There was no observed survival benefit in any group that received low dose masitinib compared to placebo, regardless of baseline disease severity and/or disease progression rate.

During the unblinded follow-up period post data readout, patients could choose to join the optional, open-label Named Patient Program (NPP), which allowed patients receiving masitinib to continue on the drug, as well as for placebo-arm patients to initiate masitinib treatment. This led to further groups for overall survival analysis. Similar rates of each group participated in this program, with 23% and 22% of the low and high dose masitinib groups, respectively, continuing treatment, and 19% of the placebo arm switching to masitinib treatment. This program also yielded a subgroup of the placebo group (40%) that did not opt into the NPP program and thus were masitinib naïve for the duration of the study and follow-up. When the researchers compared those who received high dose masitinib for the original study and follow-up (n=29) compared to the masitinib-naïve placebo patients (n=53) regardless of baseline disease severity or progression rate, there was a significant 11-month difference in median overall survival, favoring masitinib (p=0.008). There was also a significant survival benefit for the pooled group of participants who received low or high dose of masitinib in the original trial compared to those who never received masitinib (p=0.008) and for anyone who received masitinib, including those who switched from placebo to masitinib through the NPP program, compared to those who never received masitinib (p=0.016).

Two pre-print articles have reported further analyses from the original trial. The not-yet peer reviewed [Ludolph et al., 2025](#) describes a re-review of the baseline characteristics of AB10015 and identifies a previously unrecognized imbalance. The researchers state that compared to the placebo group, the high dose masitinib group had a higher proportion of patients with 'very severe loss of functionality' as defined as at least one ALSFRS-R score of zero (8% vs. 20%, respectively). They therefore performed a post-hoc analysis that only included patients with scores of at least 1 on every item of the ALSFRS-R in placebo (n=104) and masitinib (n=84). These post-hoc groups were said to be well-matched. The analyses suggested a benefit of high dose masitinib in terms of ALSFRS-R scores (p=0.0065), a median gain of 5 months of progression free survival (p=0.0057), and a median overall survival gain of 6 months

($p=0.0192$). Another pre-print by [Ludolph et al., 2026](#) reports a post-hoc analysis that the high dose masitinib group showed a higher 5-year survival rate compared to historical benchmark data, particularly in those with normal progression rates. They also report that half of their long-term survivors had satisfactory quality of life as defined by no requirement for mechanical assistance such as wheelchair, permanent ventilation, or tracheostomy.

Several regulatory agencies have declined to approve masitinib, citing concerns with the trial protocol and data analysis ([ALS News Today](#)), as well as the medication production and significant attrition ([EMA](#)). AB Science plans to run a confirmatory phase 3 trial in response (see 'Research Underway' for further details).

MS

A phase 3 RCT known as AB07002 assessed the efficacy of two doses of masitinib in patients with MS. The trial randomized 611 patients with primary progressive MS or nonactive secondary progressive MS without relapse for at least 2 years to receive either 4.5 mg/kg per day masitinib or uptitrated 6.0 mg/kg per day masitinib or matching placebo for 96 weeks. The trial had an additional 45 enrollees who were originally randomized to a 6 mg/kg masitinib per day dose that was not titrated; this arm of the study was halted early and not analyzed. The uptitrated 6 mg/kg arm was added after the early stop of the 6 mg/kg starting dose arm, and thus was run as an independent, parallel study with its own placebo group. The primary outcome was the change in the Expanded Disability Score (EDSS), which is a measure of MS disease severity. At the end of the trial, the 4.5 mg/kg masitinib group had significantly less decline on the EDSS than the matching placebo group (LSM= -0.097 ; 97% CI -0.192 to -0.002 ; $p=0.026$). Patients who received masitinib were also 39% more likely to have either disease improvement or disease stabilization compared to placebo (OR=0.610; 95% CI 0.376 to 0.988, $p=0.045$). However, there was no similar significant difference in the uptitrated 6 mg/kg masitinib group in disease progression. The researchers ascribe this to an atypical improvement in placebo group for the uptitration arm of the study ([Vermersch et al., 2022](#)).

An earlier pilot study in MS tested doses of 3 to 6 mg/kg of masitinib per day for at least 12 months in 35 patients with primary progressive MS or relapse-free secondary progressive MS. The protocol allowed dose increases, and a vast majority of the patients were dose escalated to 6 mg/kg per day; thus, the results effectively pooled the masitinib group into one. There was a positive though non-significant trend towards a benefit of masitinib compared to placebo as measured by multiple sclerosis functional

composite score (MSFC), with 7 of 22 masitinib patients reporting clinical response compared to 0 of 6 in the placebo group. This trial was originally planned to analyze results from 35 patients with a 36-month treatment period; they amended this to analyze at least 20 patients who had completed at least 12 months of treatment ([Vermersch et al., 2012](#)).

Mechanisms of action for neuroprotection identified from laboratory and clinical research:

Neuroinflammation is a common pathological feature of neurodegenerative diseases. Significant research attention has been devoted to microglia and astrocytes. The role of peripheral immune cells such as mast cells in disease has been less well explored, but there is evidence of potential involvement.

Studies of postmortem brain tissue from patients with AD show higher numbers of mast cells than samples from controls ([Jones et al., 2019](#)). A preclinical study crossed 5XFAD mice with a mouse strain deficient in mast cells and found that 5XFAD mice that lacked mast cells had improvements in contextual fear conditioning compared to 5XFAD mice with mast cells. They also found that mast cell deficient 5XFAD mice had reduced markers of reactive astrocytes and increased microglial transcriptomic signatures thought to be neuroprotective compared to 5XFAD mice with mast cells. It should be noted that mast cell deficiency did not improve anxiety-like behavior or amyloid deposition, nor did it lower levels of proinflammatory cytokines like IL-1 β ([Lin et al., 2023](#)).

Treating 12-month-old AD model APPPS1dE9 mice with masitinib for 2.5 months improved spatial learning and led to increases in the synaptic marker synaptophysin compared to vehicle treated mice. The researchers saw a similar effect on synaptophysin levels in APPPS1dE9 mice with knock-down of c-kit expression. They did not observe any decrease in amyloid load or inflammatory markers such as IL-1 β ([Li et al., 2020](#)). Another study used an acrolein-induced mouse model of sporadic AD and treated mice with masitinib. They reported that masitinib treatment led to significant improvements in learning and memory, anxiety-like behaviors, and acrolein-induced olfactory dysfunction compared to control mice. They also reported that masitinib treatment reduced levels of phosphorylated tau and increased expression of PSD95 as well as restored density of dendritic spines ([Jia et al., 2025](#)).

Masitinib has also been tested in preclinical models of other diseases. In the experimental autoimmune encephalitis (EAE) mouse model, treatment with masitinib after induction of EAE resulted in improvements in motor function and reduced serum neurofilament light chain levels as well as other pro-inflammatory cytokines compared to vehicle treatment ([Hermine et al., 2025](#)). As discussed in the

scoping review by [Hamad et al., 2024](#), treatment with masitinib mitigated neurological deficits and reduced infarct size in animal models of stroke. In different studies of animal models of ALS, treatment with masitinib mitigated neuroinflammation and motor neuron pathology, prolonged post-paralysis survival in paralyzed rats, promoted reinnervation and improved motor function.

While the effect of masitinib on mast cells via its inhibition of c-kit is well appreciated, masitinib has inhibitory activity towards other tyrosine kinases which could also contribute to any neuroprotective activity of masitinib. For instance, masitinib has been reported to inhibit CSF1R thus may modulate microglia ([Trias et al., 2016](#)). Masitinib also has activity against Fyn, which has been reported to mediate tau deposition as well as A β toxicity ([Briner et al., 2020](#)). Further work is needed to validate these initial findings.

APOE4 interactions:

It is not known whether masitinib would have differential effects based on APOE status.

Aging and related health concerns: Masitinib has been tested in different cancer subtypes and for rheumatoid arthritis, severe asthma, and COVID-19. Despite some reports of positive results, development for these indications has not continued.

Types of evidence:

- 1 network meta-analysis
- 3 clinical trials
- 1 press release
- 1 laboratory study

Masitinib has been tested for several potential indications but is not currently being developed for any non-neurological age-related disease.

Masitinib has been tested in an RCT with gemcitabine for advanced pancreatic cancer ([Deplanque et al., 2015](#)) and a network meta-analysis of RCTs found that this combination was ranked second by SUCRA in terms of overall survival ([Ma et al., 2025](#)). It has been tested in an open-label trial for gastrointestinal stromal tumor (GIST) after failure of imatinib ([Adenis et al., 2014](#)).

Masitinib has been tested for rheumatoid arthritis in a small open-label trial of 43 patients. Dosing was randomized and ranged from 3 to 6 mg/kg per day and lasted for 12 weeks. While there were improvements in efficacy endpoints such as the score on an assessment of rheumatoid arthritis symptoms, no placebo-controlled trial was run to follow up on these preliminary findings ([Tebib et al., 2009](#)).

A trial in 419 adults with severe asthma compared add-on therapy of 6 mg/kg per day of masitinib to placebo. The average drug exposure duration was 13 months. They found that masitinib treatment met the primary endpoint of significantly decreasing the annualized severe asthma exacerbation rate by 35% (RR=0.65; 95% CI 0.47 to 0.90, p=0.010) ([Davidescu et al., 2022](#)).

A trial was initiated to explore the utility of masitinib vs placebo as an add-on therapy to isoquercetin for hospitalized patients with COVID-19 ([NCT05047783](#)). The company announced that the trial was unable to recruit the planned 200 patients and halted at 95, and that they observed an improvement in clinical status in treated patients compared to placebo in a press release ([AB Science](#)). These results do not appear to be published, and AB Science indicates that they are no longer developing masitinib for COVID-19 ([AB Science Pipeline](#)).

Safety: Common adverse events of masitinib include rash, gastrointestinal events, abnormal lab values like neutropenia, and edema. Elevated transaminases have been seen. These events are serious and lead to study discontinuation more often than placebo.

Types of evidence:

- 1 meta-analysis
- 1 clinical trial
- 1 case report
- 3 news articles
- 2 press releases
- 1 laboratory study

Masitinib has been tested for several different health conditions, and trials do not all report the same safety events. Common adverse events appear to be rash, gastrointestinal symptoms like vomiting,

nausea, and diarrhea, abnormal lab values like neutropenia, and peripheral and eyelid edema ([Salvado et al., 2015](#)). Elevated liver enzymes have been reported in several trials.

The safety profile of masitinib in patients with neurodegenerative diseases was meta-analyzed by [Hamad & Amer, 2024](#). The meta-analysis included 5 RCTs (n=1,781): 2 in MS, 2 in AD, and 1 in ALS. The studies tested doses of 3, 4.5, and 6 mg/kg of masitinib per day compared to placebo; some of the trials, such as the AD and ALS trials, tested masitinib as an add-on therapy to the standard of care therapy. Trial duration ranged from 24 weeks to 96 weeks. The researchers found that regardless of masitinib dose, the masitinib groups had a higher incidence of adverse events (RR=1.12; 95% CI 1.07 to 1.17, $p<0.01$) and severe adverse events (RR=1.36; 95% CI 1.07 to 1.73, $p=0.01$) compared to the placebo group. There was low heterogeneity observed for all of these findings. The masitinib group had a significantly higher incidence of non-fatal serious adverse events as well as adverse events leading to dose reduction or discontinuation. There was no significant difference between groups in adverse events leading to death (RR=0.87; 95% CI 0.47 to 1.61, $p<0.66$). Subgroup analyses investigated the incidence of adverse events by dose for 3 and 4.5 mg/kg per day of masitinib; the 6 mg/kg per day dose could not be assessed due to heterogeneity in administration in the included studies. These subgroup analyses found that the incidence rate of any adverse event as well as an adverse event that led to treatment discontinuation was significantly higher in the masitinib group compared to placebo group, regardless of dose of masitinib. There was no difference in incidence of severe adverse events or non-fatal serious adverse events between the 3 mg/kg masitinib group and placebo, while there was a significant increase in the incidence of both of these types of events in the 4.5 mg/kg masitinib group compared to placebo (severe adverse event RR=1.50; 95% CI 1.14 to 1.98, $p<0.01$; non-fatal serious adverse event RR=1.84; 95% CI 1.36 to 2.50, $p<0.01$).

The meta-analysis by [Hamad & Amer, 2024](#) did not include any details on the specific types of adverse events. The following trials were included in the meta-analysis, and the details on the types of adverse events they reported are below.

- [Dubois et al., 2023](#) details the findings of a phase 3 trial of masitinib in 718 patients with mild-to-moderate AD. Originally, patients were to be randomized to either placebo or 6 mg/kg per day of masitinib. However, ongoing safety analyses of masitinib trials around the world suggested that a starting dose of 6 mg/kg had an increased risk of certain adverse events compared to placebo, whereas a starting dose of 3 mg/kg or 4.5 mg/kg did not have an increased risk of these adverse events. The 6 mg/kg arm was therefore discontinued and



replaced with a 3 mg/kg arm and a 4.5 mg/kg arm. The 3 mg/kg arm was also discontinued based on a recommendation from an Independent Data Monitoring Committee; terminating the 3 mg/kg arm was not due to safety or futility concerns. All patients who received at least one dose of study medication were included in safety analyses and were compared to the pooled placebo population (n=280).

The authors report that masitinib increased the incidence of too-low levels of neutrophils, known as neutropenia, as well as other abnormal lab results, which drove the difference in incidence of overall adverse events between groups. When they looked at the differences in frequencies of non-fatal severe adverse events, neutropenia, pneumonia, and Stevens-Johnson syndrome (a rare and serious skin condition characterized by fever, rash, and blisters, followed by shedding of the skin) were all more common in the masitinib treated groups. The cases of Stevens-Johnson syndrome were all in the group that titrated up to 6 mg/kg per day, were not life-threatening, and was judged as possible rather than definite Stevens-Johnson syndrome. There were three fatalities in the trial: one in the placebo group, one in the 4.5 mg/kg per day masitinib group, and one in the titrated up to 6 mg/kg per day group. The researchers report that the deaths were not treatment-related, but do not include further details on the cause of death.

- [Piette et al., 2011](#) describes the phase 2 RCT of masitinib in patients with mild to moderate AD. The most common adverse events were edema including peripheral and eyelid edema, gastrointestinal events like diarrhea, nausea, vomiting, rash, and metabolic or general disorders. The majority of the events were mild to moderate in intensity, though 15% of masitinib-treated patients and 13% of placebo-treated patients experienced severe adverse events. The severe adverse events in the masitinib group included rash, anorexia, nausea, asthenia, and transaminase increase along with mild neutropenia and leukopenia. Treatment-related adverse events led to 27% of the masitinib group to discontinue study treatment. The researchers speculated that the discontinuations may have been due to a lower risk tolerance for side effects for a drug perceived as chemotherapeutic, though it should be noted that the withdrawals were in patients who experienced severe (n=4) or non-fatal serious adverse events (n=3).
- [Mora et al., 2020](#) details an RCT testing 3 and 4.5 mg/kg masitinib compared to placebo as an add-on therapy to riluzole in patients with ALS. Maculopapular rash and peripheral edema were

reported at least 5% more frequently in the masitinib groups compared to placebo. There was one case of autoimmune-like hepatitis with elevated liver transaminases in the high-dose masitinib arm; this study is described by [Salvado et al., 2015](#) below. Three other cases of increased transaminases were identified in the masitinib groups in this trial; all were non-severe and resolved following treatment interruption or early discontinuation.

- [Vermersch et al., 2022](#) reports on a phase 3 trial of 4.5 mg/kg and uptitrated 6 mg/kg masitinib per day. In the 4.5 mg/kg masitinib group, diarrhea, maculopapular rash, nausea, peripheral edema, pruritus, and various abnormal lab results such as anemia were among the adverse events that were at least 5% more common in the masitinib group compared to the placebo group. The most common treatment-emergent serious nonfatal adverse events included maculopapular rash, neutropenia, elevated gamma-glutamyl transferase, erythema multiforme, and palmar-plantar erythrodysesthesia syndrome (also known as hand-foot syndrome; it is characterized by swelling, redness, and blistering of the palms of the hands and soles of the feet); these events occurred in 2 or 3 patients a piece. In the uptitrated 6 mg/kg masitinib group, the most common treatment-emergent adverse event was nausea. The most common treatment-emergent serious adverse events were neutropenia and maculopapular rash. There were two deaths in the masitinib group (cellulitis and myocardial infarction) and none in the matching placebo group.
- [Vermersch et al., 2012](#) describes a pilot study of masitinib in 35 patients with MS. The most common adverse events in patients receiving masitinib were asthenia, rash, nausea, edema, and diarrhea. Some of these events, such as some cases of rash, were severe in intensity. There were also hematological events such as leukopenia, lymphopenia, and one severe case of neutropenia.

A case report was published in 2015 describing a case of autoimmune-like hepatitis in a patient with ALS who was enrolled in the study described in [Mora et al., 2020](#). The patient in the case study was on concurrent riluzole as well as vitamin E and paroxetine before the start of the trial, and she was randomized to receive 300 mg per day of masitinib. A scheduled biochemistry blood test for the week 24 visit showed elevated transaminases and bilirubin that met criteria for a severe (grade 3) elevation as per the study protocol. The patient also had nausea and jaundice. The masitinib and riluzole treatments were discontinued. The transaminase levels continued to rise, reaching a peak of up to 64 times her baseline value. Further laboratory tests and biopsies suggested an acute drug-induced liver injury with



autoimmune-like histological pattern. The patient started on prednisone and azathioprine; the transaminases returned to baseline level 5 months later ([Salvado et al., 2015](#)).

An RCT tested 6 mg/kg per day of masitinib vs. placebo in 419 adults with severe asthma. Participants had an average exposure of 13 months to masitinib. There was a similar incidence of overall adverse events, severe adverse events, and serious non-fatal adverse events in the two groups. There was a significantly greater incidence of trial discontinuation due to treatment-related adverse events in the masitinib group compared to placebo (RR=3.0), with 11.4% of the masitinib group permanently discontinuing compared to 3.8% of the placebo group. There were 3 deaths (1.1%) in the masitinib group due to pneumonia, ischemic stroke, and pulmonary embolism, and 1 death (0.8%) in the placebo group due to cardiopulmonary failure; none of these events were judged to be related to study treatment. Maculopapular rash, various asymptomatic abnormal laboratory results including elevated liver enzyme levels, weight loss, and gastrointestinal adverse events such as vomiting, diarrhea, nausea, and abdominal pain were more common in the masitinib group compared to placebo ([Davidescu et al., 2022](#)).

An open-label study in 43 patients with rheumatoid arthritis reported that 30% of the participants withdrew because of adverse events. Adverse events were often mild or moderate, and the most common adverse events were rash, edema, nausea, and diarrhea. However, in 21% of the patients, the adverse events were severe, including edema and rash. One patient had elevated liver enzymes ([Tebib et al., 2009](#)).

In a phase 3 RCT in adults with indolent or smoldering systemic mastocytosis, 135 patients were randomized to receive 6 mg/kg per day of masitinib or placebo for 24 weeks with a 96-week extension phase. All patients in the trial experienced at least one adverse event in the 24-week treatment period. There was one death in the placebo group. Compared to the placebo group, the masitinib group had a higher incidence of non-fatal serious adverse events (29% vs. 19%), severe adverse events (50% vs. 35%) and an adverse event leading to permanent discontinuation (24% vs. 6%), respectively. The most common severe adverse events were diarrhea, rash, asthenia, edema, and neutropenia, and all were all more common in the treatment group compared to the placebo group (placebo vs. masitinib frequencies: diarrhea 2% vs. 11%; rash 0% vs. 6%; asthenia 2% vs. 6%; edema 0% vs. 4%; pruritic 2% vs. 4%). When the researchers looked at the long-term extension data, they found a similar rate of adverse events when analyzed as incidence per patient-months of exposure ([Lortholary et al., 2017](#)).

In June 2021, AB Science placed a voluntary hold on new patient enrollment for studies due to a potential safety signal for ischemic heart disease. This safety signal came from an exploratory safety analysis of a subset of studies and a subset of patients; the analysis, performed by AB Science, found an imbalance of ischemic heart disease between masitinib and placebo groups which theoretically could signal a risk of masitinib. They performed meta-analyses, which did not confirm the signal. AB Science then shared these data with relevant medical authorities, who performed independent investigations. During these investigations, AB Science put a hold on new enrollments though they continued to dose patients already enrolled, provided positive individual risk/benefit was documented ([AB Science](#)). While details on the final analysis were not identified, French authorities cleared AB Science to resume enrollment in September 2021 with new safety measures in place, such as exclusion of patients with history of severe cardiovascular disease and more monitoring for cardiac side effects. Other European countries came to similar decisions ([ALS News Today](#)). AB Science has since been cleared to start new trials ([ALS News Today](#)).

Drug interactions:

The drug interactions of masitinib in humans are not fully understood.

Patients treated with masitinib and cytochrome P450 3A4 inhibitors should be monitored ([Salvado et al., 2015](#)).

Research underway:

[Clinicaltrials.gov](#) indicates that there are 3 active or soon-to-be active registered trials of masitinib. All three are for neurodegenerative conditions.

[NCT05564169](#) is a randomized controlled phase 3 trial to assess the safety and efficacy of masitinib as an add-on therapy for patients with mild AD. The study plans to enroll 600 patients with mild AD and randomize them to receive either masitinib (3 mg/kg per day, dose escalated up to 4.5 mg/kg per day after 4 weeks of treatment) or matching placebo by mouth twice daily. All patients will be given masitinib as an add-on therapy to the standard-of-care treatment of cholinesterase inhibitors and/or memantine at their standard-of-care doses. Dosing will last for 24 weeks, with a 24-week extension phase. The primary outcome measure is the change in iADRS score from baseline to 24 weeks. Other

outcome measures include changes in cognitive assessments like MMSE, ADAS-Cog, and CDR, daily functioning as assessed by ADCS-ADL, and psychiatric symptoms as assessed by the Neuropsychiatric Inventory (NPI). This study is estimated to begin in June 2026 and complete at the end of 2029.

[NCT03127267](#) (AB19001) is a randomized controlled phase 3 study of masitinib in patients with ALS run by AB Science. The trial aims to enroll 495 patients with ALS and randomize them to receive twice daily low dose masitinib (starting dose 3 mg/kg per day, dose escalation to 4.5 mg/kg after 4 weeks), twice daily high dose masitinib (starting dose 3 mg/kg per day, first dose escalation to 4.5 mg/kg per day after 4 weeks of treatment, second dose escalation to 6.0 mg/kg per day after a further 4 weeks of treatment), or matching placebo. All three groups will also receive 50 mg riluzole twice daily. Dosing will last for 48 weeks. The primary outcome measure is the change in ALSFRS-R, an assessment of ALS disease severity, from baseline to end of dosing. Secondary outcome measures include progression-free survival as defined by time from randomization to disease progression or death, measures of respiratory function and muscle strength, and quality of life. The trial started in 2021 and was set to complete at the end of 2027.

However, NCT02588677 had recruitment struggles ([ALS News Today](#)). Upon advice of US and European regulators, a new study was designed to overcome the barriers to recruitment.

[NCT07174492](#) (AB23005) is a second randomized controlled phase 3 trial of masitinib in patients with ALS run by AB Science. This trial plans to enroll 412 patients with ALS and randomize them to receive masitinib (3 mg/kg per day, dose escalation to 4.5 mg/kg per day after 4 weeks of treatment) or placebo. Patients will also receive riluzole in both groups; all medication is taken by mouth twice a day for a total of 48 weeks. The primary outcome is change in ALS-FRS-R, an assessment of ALS disease severity. The secondary outcomes are progression free survival and change in quality of life. This trial was slated to begin in January 2026 and complete at the end of 2029; it is listed as “Not yet recruiting” as of May 2026.

Search terms:

Pubmed, Google: masitinib

- Alzheimer’s disease, cognitive function, ALS, MS, ischemic heart disease, safety

Websites visited for masitinib:

- [Clinicaltrials.gov](https://clinicaltrials.gov)
- [PubChem](https://pubchem.ncbi.nlm.nih.gov)
- [DrugBank.ca](https://drugbank.ca)
- [Cafepharm](https://www.cafepharm.com)

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