AB SCIENCE

Corporate Presentation

January 2023

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Overview

Management Team

ALAIN MOUSSY
Co-founder and CEO

Former strategic consultant at Booz, Allen & Hamilton and former Head of Corporate Development at Carrefour.
President of AFIRMM, association of mastocytosis patients

OLIVIER HERMINE, MD, PhD
Co-founder and Chairman of Scientific Committee

Member of the French Académie des Sciences and author of 700 international publications

CHRISTIAN FASSOTTE, MD
Chief Medical Officer

Medical Doctor. 30 years of experience, including executive position at Sanofi for Medical, Regulatory Affairs and R&D

LAURENT GUY
Chief Financial Officer

Former positions in the banking industry (Société Générale and Paribas) and strategy consulting (Accenture).

Stock Information

- Listed on Euronext Compartment B
- ISIN : FR0010557264
- Tickers : AB.PA (Reuters) ; AB:FP (Bloomberg)
- Shares outstanding : 53,199,453 (https://www.ab-science.com/investors/regulated-information/monthly-disclosure-of-total-outstanding-shares-and-voting-rights/)
- Website : https://www.ab-science.com/
- Head Office : Paris, France

Pipeline

AB Science has a diversified and late-stage portfolio with masitinib being a platform

Compound	Class	Therapeutic area	Indication	Preclinical	Phase 1	Phase 2	Phase 2B/3	Confirmatory Phase 3	Conditional Approval
Masitinib	Tyrosine Kinase Inhibitor (TKI) (oral)	Neurology Diseases	Amyotrophic Lateral Sclerosis*	*On-going confimatory study*					*Under review in Canada and EU*
			Alzheimer's Disease*	*On-going confimatory study*					
			Progressive forms of Multiple Sclerosis*	*On-going confimatory study*					
		Inflammatory Diseases	Indolent Systemic Mastocytosis*	*On-going confirmatory study*					
			Mast Cell Activation Syndrome	*Authorized phase 2*					
			Severe Asthma Uncontrolled *	*First phase 3 completed*					
		Oncology	**Metastatic Prostate Cancer castrate resistant eligible to chemotherapy ***	*First phase 3 completed*					
			Locally Advanced Pancreatic Cancer with pain*	*First phase 3 completed*					
		Viral Diseases	COVID-19 (hospitalized and non-hospitalized at high risk)	*Two on-going phases 2*					
AB8939	Microtubule destabilizer (IV)	Oncology	Refractory Acute Myeloid Leukemia	*On-going phase 1/2*					
ABXXXXX	Microtubule destabilizer (oral)	Oncology	Sarcoma, solid tumors						
ABYYYYY	TKI (oral)	Inflammatory Diseases	Mastocytosis						

** Positive Results Reported*

Masitinib

Masitinib has a blockbuster potential in unmet medical needs, both in large and orphan diseases

Therapeutic area	Indications	Estimated Annual Nber of patients (USA and EU)	Available treatments	Annual Treatment List Price (in USD)
Neurology Diseases	Alzheimer's disease	5 000 000	Aduhelm (in early AD)	28,200 *(Aduhelm)*
	Progressive forms of Multiple Sclerosis	500 000	Ocrevus (in PPMS)	68,100 *(Ocrevus)*
	Amyotrophic Lateral Sclerosis	50 000	Radicava, Relyvrio	154,000 *(Relyvrio)*
Inflammatory Diseases	Mast Cell Activation Syndrome	500 000	None	Not available
	Severe Asthma uncontrolled by OCS	70 000	Multiple options	37,000 *(Dupixent)*
	Indolent Systemic Mastocytosis	65 000	None	Not available
Oncology	Metastatic Prostate Cancer castrate resistant eligible to chemotherapy	125 000	None (combo with docetaxel)	139,600 *(Zytiga)*
	Locally advanced pancreatic cancer with pain	40 000	Abraxane, folfirinox	170,600 *(Abraxane)*
Viral Diseases	Covid-19 (hospitalized and non-hospitalized at high risk)	Multiple millions	Paxlovid, molnupiravir	700 per 5-day course *(Paxlovid)*

Indications listed by decreasing order of number of patients

Masitinib

Masitinib core development is in Central Nervous System

Rationale

Modulation of
- Microglia
- mast cells

Neuro-protection of central and peripheral nervous system

Indications	Large phases 2B/3 completed	Phase 2B/3 Publication	On-going confirmatory phases 3
Amyotrophic lateral sclerosis	• 394 patients enrolled. • Primary endpoint met • ID : NCT02588677	• Mora 2020 (main study) • Mora 2021 (long-term survival)	• Actively Recruiting (USA & EU) • 495 patients • ID : NCT0312726
Progressive forms of multiple sclerosis	• 656 patients enrolled. • Primary endpoint met ID : NCT01433497	• Vermersch 2022	• Actively Recruiting (USA & EU) • 800 patients • ID : NCT05441488
Alzheimer's disease	• 720 patients enrolled. • Primary endpoint met • ID : NCT01872598	• pending	• Recruitment initiated (USA & EU) • 600 patients • ID : NCT05564169

3 pivotal phases 2B/3 studies testing 3 doses of masitinib met their primary endpoint at the same dose of 4.5 mg/kg/day

Amyotrophic lateral sclerosis

Phase 2B/3 demonstrated with masitinib 4.5 mg/kg/day a significant delay of disease progression over a 48-week period in the primary analysis population and significant OS benefit in subgroup of patients with moderate ALS

Normal Progressors (Primary Endpoint) : 27% slowing of functional deterioration

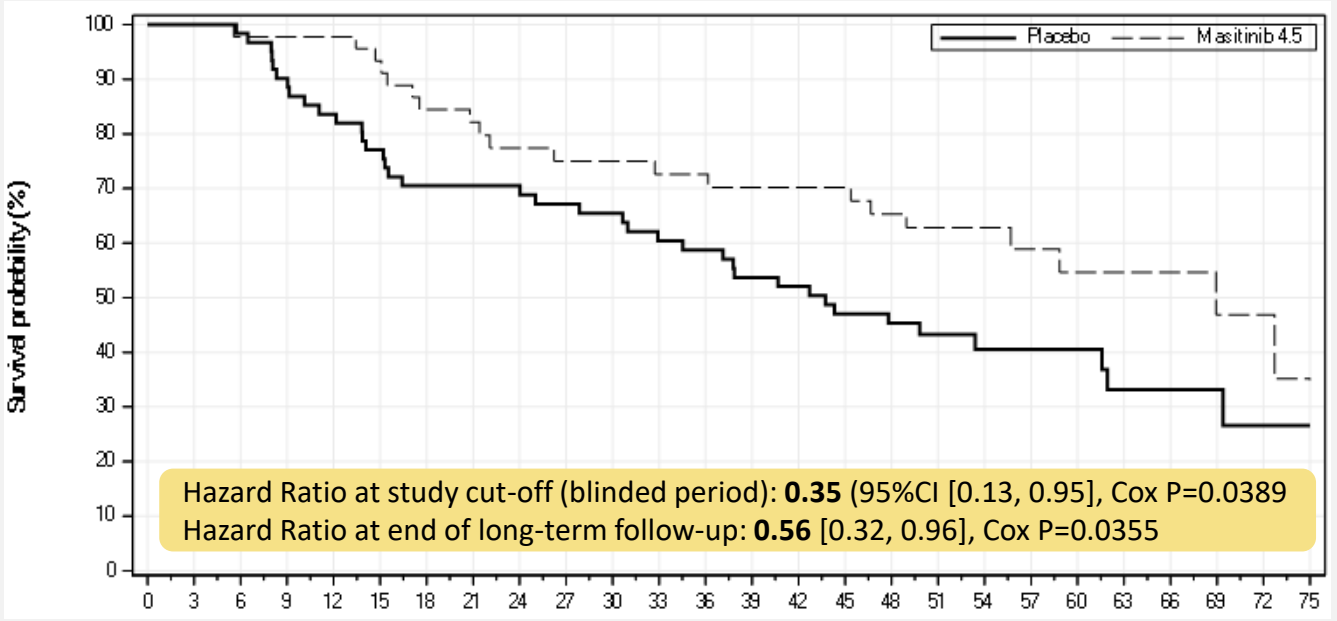
PRIMARY ANALYSIS
Absolute change from baseline to week 48 in ALSFRS-R
masitinib 4.5 mg/kg/day – Normal Progressors

Treatment group	Difference of means	[95% CI]	p-value
Primary Analysis			
LOCF Method	3.39	[0.65;6.13]	0.0158
Sensitivity analyses imputing all missing data			
Multiple Imputation Model (Proc MI)	3.44	[0.54; 6.33]	0.020
Multiple Imputation with Penalty (J2R)	2.80	[0.15; 5.46]	0.0386

* Defined as Normal Progressors with baseline score ≥ 2 on each ALSFRS-R item

+ 25 months in median OS for patients with moderate ALS

POST-HOC SUBGROUP ANALYSIS
Kaplan–Meier survival curves from pivotal phase 3 study long-term survival analysis in Moderate ALS patients* - Masitinib 4.5 mg/kg/d – June 2020 cut-off)

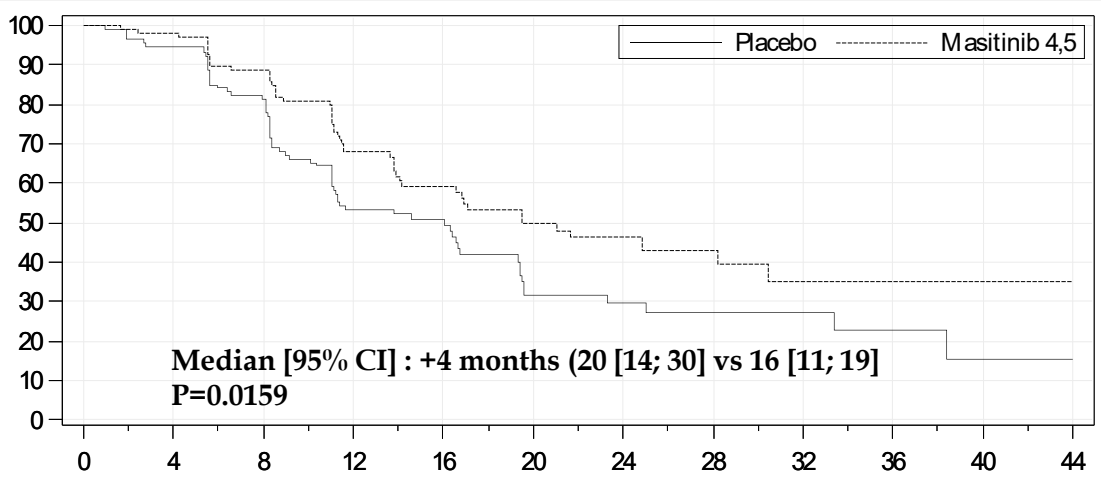


65% reduction of risk of death

Amyotrophic Lateral Sclerosis

Benefit on functional score (ALSFRS-R) was supported by improvement in secondary endpoints in (time to disease progression or death (PFS), quality of life, and respiratory function)

25% delay in disease progression (PFS): +4 months



PFS (Progression Free Survival) is a time to event endpoint, with the event defined as the earliest between death or a 9-point deterioration of ALSFRS-R from baseline

28% improvement in quality of life

ALSAQ-40 score – Masitinib 4.5 mg/kg/day – Normal Progressors

Treatment group	LS Mean	Diff.of means [95% CI]	p-value
Control	27.2	-7.8 [-13.45;-2.06]	0.0078
Masitinib 4.5 mg/kg/d	19.4		

Quality of Life Component	Diff. of means [95% CI]	p-value
Eating and drinking	-13.70 [-22.14; -5.26]	0.0016
Activities of daily living and independence	-10.23 [-17.68; -2.78]	0.0074
Communication	-9.21 [-17.36; -1.07]	0.0269
Physical mobility	-7.53 [-15.06; -0.01]	0.0497
Emotional reactions	-2.85 [-10.14; 4.44]	0.4418

22% improvement in respiratory function

FVC – Masitinib 4.5 mg/kg/day – Normal Progressors

Treatment group	LS Mean	Diff.of means [95% CI]	p-value
Control	-33.99	7.55 [0.75;14.32]	0.0296
Masitinib 4.5 mg/kg/d	-26.45		

Amyotrophic Lateral Sclerosis

Results from phase 2B/3 and long-term survival were published in two peer-reviewed journals

Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration, 2020; 21: 5–14

Taylor & Francis
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RESEARCH ARTICLE

Masitinib as an add-on therapy to riluzole in patients with amyotrophic lateral sclerosis: a randomized clinical trial

Abstract

Objective: To assess masitinib in the treatment of ALS. *Methods:* Double-blind study, randomly assigning 394 patients (1:1:1) to receive riluzole (100 mg/d) plus placebo or masitinib at 4.5 or 3.0 mg/kg/d. Following a blinded transition from phase 2 to phase 2/3, a prospectively defined two-tiered design was implemented based on ALSFRS-R progression rate from disease-onset to baseline (ΔFS). This approach selects a more homogeneous primary efficacy population ("Normal Progressors", ΔFS < 1.1 points/month) while concurrently permitting secondary assessment of the broader population. Primary endpoint was decline in ALSFRS-R at week-48 (ΔALSFRS-R), with the high-dose "Normal Progressor" cohort being the prospectively declared primary efficacy population. Missing data were imputed *via* last observation carried forward (LOCF) methodology with sensitivity analyses performed to test robustness. *Results:* For the primary efficacy population, masitinib ($n = 99$) showed significant benefit over placebo ($n = 102$) with a ΔALSFRS-R between-group difference (ΔLSM) of 3.4 (95% CI 0.65–6.13; $p = 0.016$), corresponding to a 27% slowing in rate of functional decline (LOCF methodology). Sensitivity analyses were all convergent, including the conservative multiple imputation technique of FCS-REGPMM with a ΔLSM of 3.4 (95% CI 0.53–6.33; $p = 0.020$). Secondary endpoints (ALSAQ-40, FVC, and time-to-event analysis) were also significant. Conversely, no significant treatment-effect according to ΔALSFRS-R was seen for the broader "Normal and Fast Progressor" masitinib 4.5 mg/kg/d cohort, or either of the low-dose (masitinib 3.0 mg/kg/d) cohorts. Rates of treatment-emergent adverse events (AEs) (regardless of causality or post-onset ΔFS) were 88% with masitinib 4.5 mg/kg/d, 85% with 3.0 mg/kg/d, and 79% with placebo. Likewise, rates of serious AE were 31, 23, and 18%, respectively. No distinct event contributed to the higher rate observed for masitinib and no deaths were related to masitinib. *Conclusions:* Results show that masitinib at 4.5 mg/kg/d can benefit patients with ALS. A confirmatory phase 3 study will be initiated to substantiate these data.

Keywords: Clinical trials, therapy, tyrosine kinase inhibitor, masitinib

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*AB10015 STUDY GROUP collaborators (non-author investigators) listed in Supplementary Table 1.

Supplemental data for this article can be accessed here.

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Therapeutic Advances in Neurological Disorders — *Original Research*

Long-term survival analysis of masitinib in amyotrophic lateral sclerosis

Jesus S. Mora, Walter G. Bradley, Delia Chaverri, María Hernández-Barral, Javier Mascias, Josep Gamez, Gisella M. Gargiulo-Monachelli, Alain Moussy, Colin D. Mansfield, Olivier Hermine and Albert C. Ludolph

Abstract

Background: A randomized, placebo-controlled phase III study (AB10015) previously demonstrated that orally administered masitinib (4.5 mg/kg/day) slowed rate of functional decline, with acceptable safety, in amyotrophic lateral sclerosis (ALS) patients having an ALS Functional Rating Scale-revised (ALSFRS-R) progression rate from disease onset to baseline of <1.1 points/month. Here we assess long-term overall survival (OS) data of all participants from study AB10015 and test whether a signal in OS is evident in an enriched patient population similar to that prospectively defined for confirmatory study AB19001.
Methods: Survival status of all patients originally randomized in AB10015 was collected from participating investigational sites. Survival analysis (using the multivariate log-rank test and Cox proportional hazards model, with stratification factors as covariates) was performed on the intention-to-treat population and enriched subgroups, which were defined according to initial randomization, baseline ALSFRS-R progression rate and baseline disease severity.
Results: A significant survival benefit of 25 months ($p = 0.037$) and 47% reduced risk of death ($p = 0.025$) was observed for patients receiving 4.5 mg/kg/day masitinib ($n = 45$) *versus* placebo ($n = 62$) in an enriched cohort with ⩾2 on each baseline ALSFRS-R individual component score (i.e. prior to any complete loss or severe impairment of functionality) and post-onset ALSFRS-R progression rate <1.1 (i.e. exclusion of very fast progressors) [median OS of 69 *versus* 44 months, respectively; hazard ratio, 0.53 [95% CI (0.31–0.92)]]. This corresponds to the population enrolled in confirmatory phase III study, AB19001.
Conclusions: Analysis of long-term OS (75 months average follow-up from diagnosis) indicates that oral masitinib (4.5 mg/kg/day) could prolong survival by over 2 years as compared with placebo, provided that treatment starts prior to severe impairment of functionality.
This trial was registered at www.ClinicalTrials.gov under identifier NCT02588677 (28 October 2015).

Keywords: clinical trials, masitinib, therapy, tyrosine kinase inhibitor

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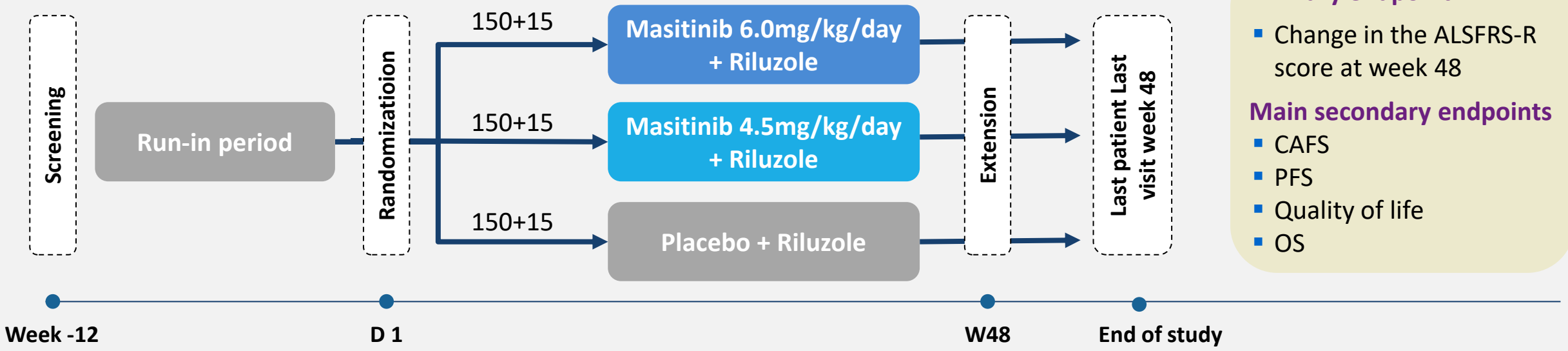
Amyotrophic Lateral Sclerosis

Confirmatory phase 3 study is authorized by FDA and key European countries and actively enrolling patients



Primary endpoint

- Change in the ALSFRS-R score at week 48

Main secondary endpoints

- CAFS
- PFS
- Quality of life
- OS

Main inclusion criteria:

- Disease duration ≤ 24 months
- Moderate ALS (Baseline functional score ≥ 2 on each ALSFRS-R items
- Exclusion of slow progressors (less than a 1-point decline during run-in perido), and fast progressors (more than a 4-point decline during run-in perido).

Randomization

- 450 moderate progressors
- Randomization 1:1:1
- 45 fast progressors included for exploratory analysis

Extension at week 48

- In case of an individual positive benefit-risk assessed by the investigator.
- Study drug dispensation in extension will end 3 months before the last patient last visit of the main period

Amyotrophic Lateral Sclerosis

There is a need for combination of treatments in ALS due to the multifactorial nature of the disease and Masitinib is the only drug with confirmatory trial having the same duration at week 48 as the first pivotal study

Status	Drug	Mechanism of action	Development plan		
			First pivotal study	**Confirmatory study**	**OS Benefit**
Approved	• Riluzole • Edaravone (IV/Oral) • AMX0035	• Unknown • Anti-oxidative stress • Anti-apoptotic	• Completed • Completed (week 24) • Completed (week 24)	• NA • **On-going (week 48)** • **On-going (week 48**)	• +3 months • No • +10.6 months
Under review	• Masitinib • Tofersen	• Anti-inflammatory & immunomodulation • Gene therapy (familial ALS)	• **Completed (week 48)** • Completed (week 24)	• **On-going (week 48)** • NA	• +25 months in moderate ALS • No
Other drugs of interest	• Ibudilast • Methylcobalamin* • CNM-Au8	• Anti-inflammatory • Anti-apoptotic • Neurotrophic factors	• Completed (week 24) • Completed (week 16) • Completed (week 24)	• **On-going (week 48)** • NA • NA	• No • No • OS benefit versus historical control

* Vitamion B12

Amyotrophic Lateral Sclerosis

Masitinib has two pending regulatory decisions in ALS for conditional approval in Europe and Canada

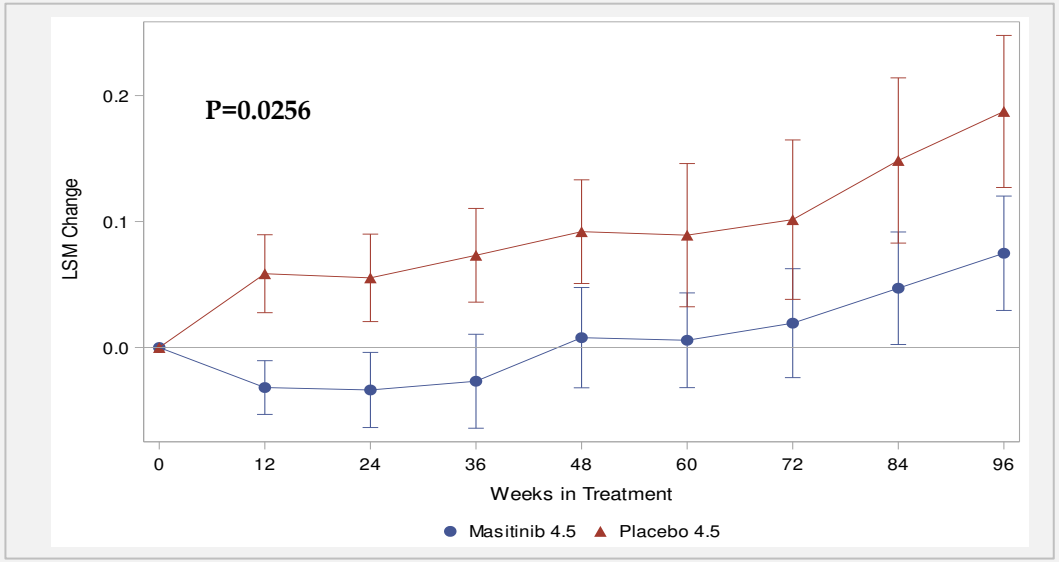
- Notice of Compliance with conditions (NOC/c) filing accepted in April 2022
- Notice of Deficiency (NOD) issued in December 2022
- AB Science intends to respond to deficiencies within 90 days

- Application filed in August 2022
- CHMP responses expected in Q3 2023

Multiple sclerosis

Phase 2B/3 demonstrated a significant benefit on disability progression with masitinib 4.5 mg/kg/day in patients with advanced stage of the disease

Significant reduction in progression on EDSS (Primary Endpoint*)



Patients were enrolled at advanced disease stage

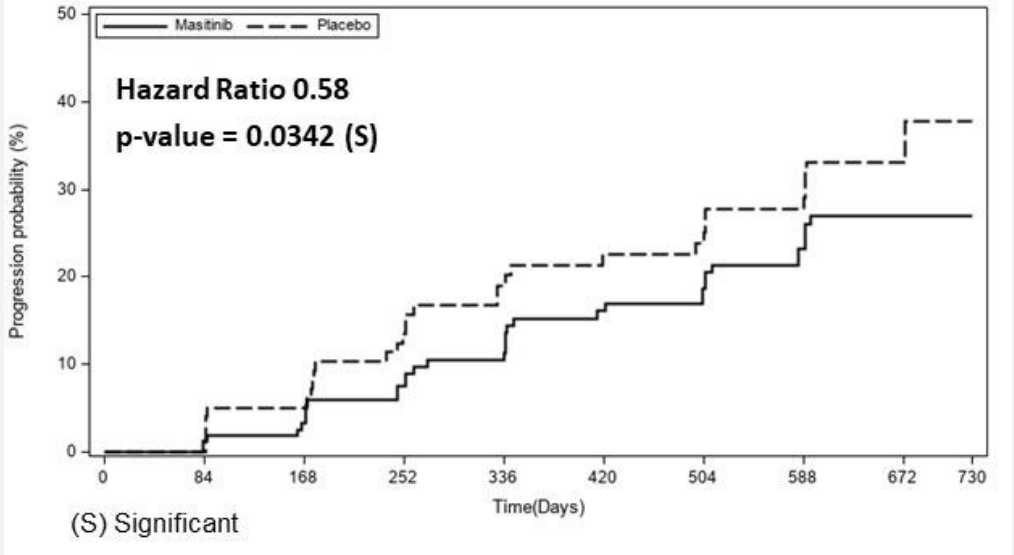
- Median age (years) : 50.0 (both masitinib and placebo)
- Median duration of first MS Symptom (yrs) :12.4 masitinib and 12.2 placebo
- Median EDSS Score :5.5 (both masitinib and placebo)
- % of patients with EDSS score of 6 :49.0% masitinib and 47.5% placebo

* Change in EDSS

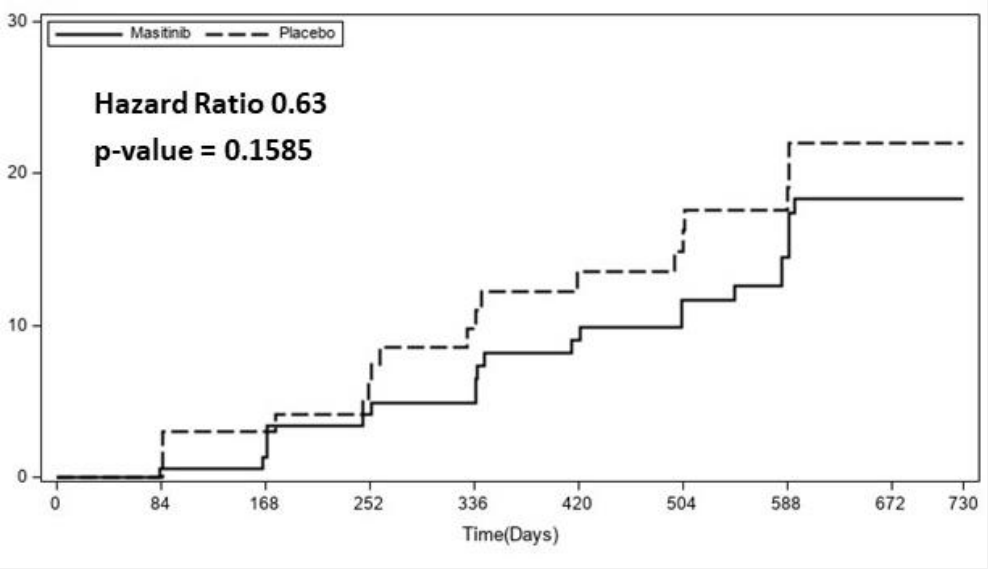
Multiple sclerosis

Phase 2B/3 demonstrated a significant reduction of risk of first disability progression by 42% and a reduction of risk of confirmed (12-week) disability progression by 37%

42% risk reduction of time to disability progression



37% risk reduction of time to confirmed disability progression



Multiple sclerosis

Masitinib has the potential to become a best-in-class drug for PPMS and nSPMS

Time to confirmed disability progression

Drug	Study Size (patients)	Type of Progressive MS	Hazard Ratio	Reduction in confirmed (3 months) disability progression
Masitinib 4.5 mg/kg/day	**300**	**PPMS and nSPMS**	**0.63**	**37% (NS)**
Ocrelizumab	**732**	**PPMS**	**0.76**	**24% (S)**
Siponimod	**1,651**	**Active SPMS**	**0.79**	**21% (S)**

S: Statistically Significant. NS : Not Statistically Significant
In masitinib study, time to confirmed disability progression was a secondary endpoint and the study was not powered to demonstrate significant effect on this endpoint

Multiple sclerosis

Results from phase 2B/3 were published in peer-reviewed journal

ARTICLE OPEN ACCESS

Efficacy and Safety of Masitinib in Progressive Forms of Multiple Sclerosis

A Randomized, Phase 3, Clinical Trial

Patrick Vermersch, MD, PhD, Luis Brieva-Ruiz, MD, Robert J. Fox, MD, Friedemann Paul, MD, PhD, Lluis Ramio-Torrenta, MD, PhD, Matthias Schwab, MD, PhD, Alain Moussy, MEng, Colin Mansfield, PhD, Olivier Hermine, MD, PhD, and Maciej Maciejowski, MD, PhD, on behalf of the AB07002 Study Group

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Neurol Neuroimmunol Neuroinflamm 2022;9:e1148. doi:10.1212/NXI.0000000000001148

Abstract

Background and Objectives

Masitinib is a selective tyrosine kinase inhibitor, targeting innate immune cells (mast cells and microglia) that are involved in the pathophysiology of progressive multiple sclerosis (MS). Study AB07002 assessed oral masitinib in patients with progressive MS who were progressing but not clinically active.

Methods

This randomized, double-blind, 2 parallel-group, placebo-controlled trial assessing 2 dose levels of masitinib vs equivalent placebo was conducted at 116 hospital clinics and specialized MS centers in 20 countries. Randomization (2:1) with minimization was performed centrally using an automated system. Patients, physicians, and outcome assessors remained masked to treatment group allocation. Patients with primary progressive MS (PPMS) or nonactive secondary progressive MS (nSPMS) without relapse for ≥2 years, aged 18–75 years, with baseline Expanded Disability Status Scale (EDSS) 2.0–6.0, and regardless of time from onset were treated for 96 weeks. The primary end point was overall EDSS change from baseline using repeated measures (generalized estimating equation, timeframe W12–W96, measured every 12 weeks), with positive values indicating increased clinical deterioration. Efficacy and safety were assessed in all randomly assigned and treated patients.

Results

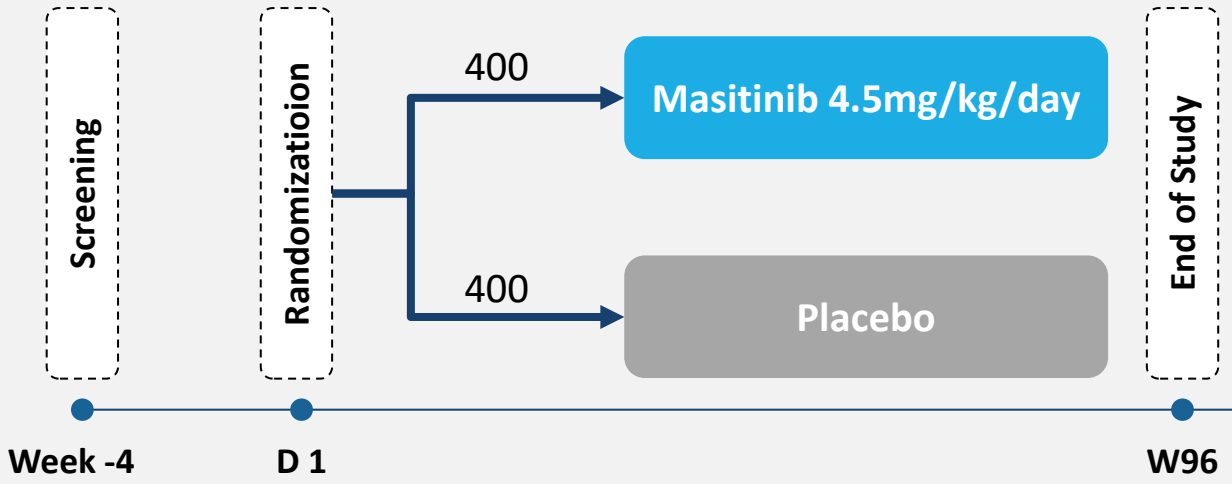
A total of 611 patients were randomized; 301 in the masitinib 4.5 mg/kg/d parallel group and 310 in the uptitrated masitinib 6.0 mg/kg/d parallel group. Masitinib (4.5 mg/kg/d) (n = 199) showed significant benefit over placebo (n = 101) according to the primary end point, 0.001 vs 0.098, respectively, with a between-group difference of −0.097 (97% CI −0.192 to −0.002); p = 0.0256. Safety was consistent with masitinib's known profile (diarrhea, nausea, rash, and hematologic events), with no elevated risk of infection. Efficacy results from the independent uptitrated masitinib 6.0 mg/kg/d parallel group were inconclusive, and no new safety signal was observed.

MORE ONLINE

Class of Evidence
Criteria for rating therapeutic and diagnostic studies
NPub.org/coe

Multiple sclerosis

Confirmatory phase 3 study is authorized by FDA and key European countries and actively enrolling patients



Primary endpoint

- Time to confirmed (12-weeks CDP) EDSS progression

Main secondary endpoints

- 24-weeks CDP
- Change in EDSS from baseline considering all measurements from baseline up to Week 96
- Time to EDSS score of 7.0
- Brain MRI Assessments

Main inclusion criteria:

- PPMS and ,nSPMS
- Onset of symptoms at least five years before inclusion
- No relapse diagnosed at least two years before inclusion (according to the 2017 revised McDonald's criteria)
- EDSS score of [3.0 to 6.0] inclusive
- Age 18 to 65 years old

Randomization

- 800 patients
- Randomization 1:1

Multiple Sclerosis

There is no approved drugs for non-active SPMS and only one for PPMS, and very few drugs into phase 3

Masitinib Positioning

Indications	Distribution of patients *(Nbr EU + USA)*	Approved treatments	Drugs in phases 3
Primary Progressive MS	**15%** (~ 150 000)	**Ocrevus (Roche) approved in 2017**	• **Masitinib** • Tolebrutinib (Sanofi) • Fenebrutinib (Roche)
Non-active Secondary Progressive MS	**35%** (~ 350 000)	**None**	• **Masitinib** • Tolebrutinib (Sanofi)
Active Secondary Progressive MS	**10%** (~ 90 000)	**16 drugs since 1993**	• Evobrutinib (Merck) • Tolebrutinib (Sanofi) • Fenebrutinib (Roche) • Remibrutinib (Novartis)
Relapsing Remitting MS	**40%** (~ 400 000)		

Masitinib
- Targets mast cells & microglia
- Positive first phase 2B/3 study

BTK inhibitors
- Targets B lymphocytes & microglia
- Tolebrutinib enrolment stopped in progressive MS due to drug-induced liver injury

All drugs in development in progressive forms of MS are TKI inhibitors

Alzheimer's disease

Phase 2B/3 study demonstrated a significant reduction in cognitive impairment based on ADAS-COG (p=0.0003) and improvement on daily activity based on ADCS-ADL (p=0.0381) with masitinib 4.5 mg/kg/day

Significant effect on cognitive function after 24 weeks of treatment

Change in ADAS-Cog - ANCOVA Analysis (Full Analysis Set) - M4.5 vs Placebo

Treatment	n	LS Mean (95% CI)	LS Mean Difference (97.51% CI)	p-value
Masitinib 4.5 mg/kg/day + memantine and anticholinesterase	182	**-1.46** (-2.46, -0.45)	**-2.15** (-3.48, -0.81)	**0.0003**
Placebo + memantine and anticholinesterase	176	**0.69** (-0.36, 1.75)		

Significant effect on daily activity after 24 weeks of treatment

Change in ADCS-Adl - ANCOVA Analysis (Full Analysis Set) - M4.5 vs Placebo

Treatment	n	LS Mean (95% CI)	LS Mean Difference (97.51% CI)	p-value
Masitinib 4.5 mg/kg/day + memantine and anticholinesterase	182	**1.01** (-0.48, 2.50)	**1.82** (-0.15, 3.79)	**0.0381**
Placebo + memantine and anticholinesterase	176	**-0.81** (-2.36, 0.74)		

Clinically relevant benefit because on top of standard of care (memantine & anticholinesterase)

Alzheimer's disease

Results from phase 2B/3 were presented at the 2021 Alzheimer's Association International Conference (AAIC)

DOI: 10.1002/alz.049866

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Masitinib in mild to moderate Alzheimer's disease: Results from study AB09004

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Abstract

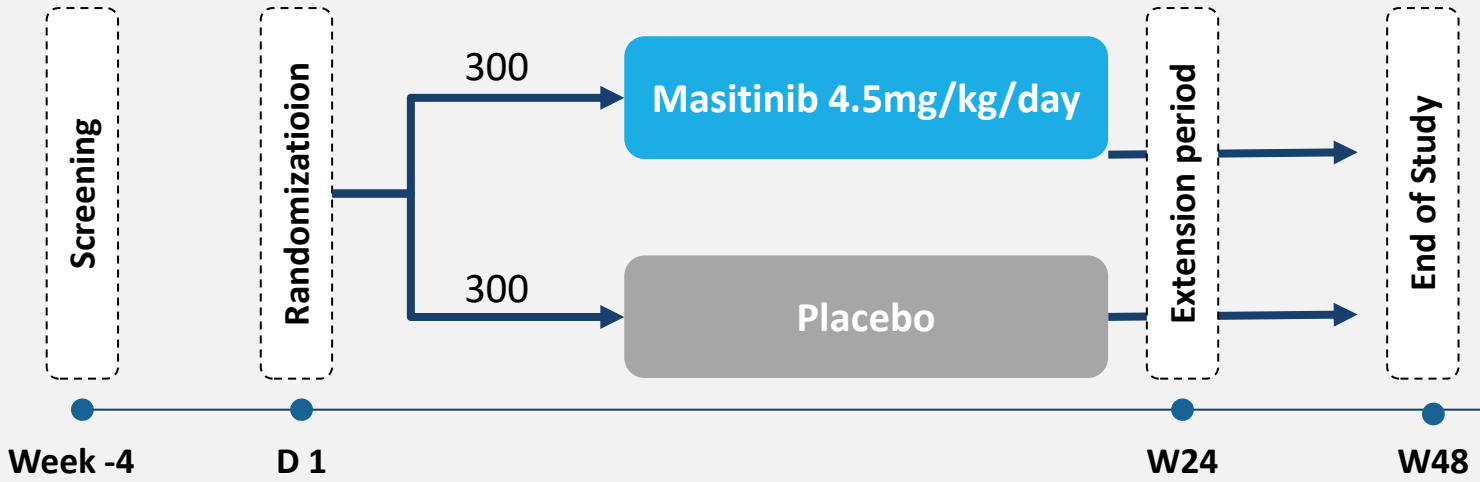
Background: Masitinib is a small molecule drug targeting KIT, LYN, FYN and CSF1R. Proof-of-concept that masitinib slowed cognitive decline in Alzheimer's disease (AD) was previously demonstrated [doi:10.1186/alzrt75; doi:10.3233/JAD-200466]. Study AB09004 assessed oral masitinib administered as an add-on therapy to standard care for the treatment of mild to moderate AD.

Method: Phase 2B/3 study AB09004 comprised two independent, double-blinded, placebo-controlled, sub-studies: masitinib at 4.5mg/kg/day versus placebo (randomized 1:1), and a titrated masitinib dose of 6.0 mg/kg/day versus matched placebo (randomized 2:1). Eligible patients that had a clinical diagnosis of AD with baseline mini-mental state examination (MMSE) score ≥12–≤25, and had received a stable dose of cholinesterase inhibitor (donepezil, rivastigmine or galantamine) and/or memantine for ≥6 months, were treated for 24 weeks. Primary endpoint was overall change from baseline at week-24 (analysis of covariance model) in the Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog) or the Alzheimer's Disease Cooperative Study Activities of Daily Living (ADCS-ADL) score. The study was successful if a significant improvement was reached on either ADAS-Cog or ADCS-ADL at a 2.5% level of statistical significance, in either sub-study.

Result: Masitinib (4.5mg/kg/day) (n=182, median (age=73 years, MMSE=19, ADCS-ADL=55.0, ADAS-Cog=25.5)) showed significant benefit over placebo (n=176, median (age=73 years, MMSE=19, ADCS-ADL=53.5, ADAS-Cog=24.8)) with a least-squares mean difference in ADAS-Cog from baseline (δCog) of -1.46 versus 0.69, respectively, and corresponding least-squares mean difference between groups (ΔCog) of -2.15 (97.5%CI[-3.48,-0.81]);p=0.0003. All ADAS-Cog sensitivity analyses were convergent with the primary outcome, including the conservative jump-to-reference approach with ΔCog of -1.89 (95%CI[-3.06,-0.72];p=0.0016). Considering ADCS-ADL, δADL was 1.01 for masitinib (4.5mg/kg/day) versus -0.81 for placebo, with a ΔADL of 1.82 (97.5%CI[-0.15,3.79]);p=0.038. Safety was consistent with the known profile for masitinib. The proportion of patients presenting at least one adverse event (AE) or severe AE was respectively, 87.0% and 26.5% for masitinib (4.5mg/kg/day, n=185) versus 77.5% and 19.3% for placebo (pooled, n=280). Efficacy results from the titrated masitinib 6.0 mg/kg/day sub-study were inconclusive and no new safety signal was observed.

Alzheimer's disease

Confirmatory phase 3 study is authorized by FDA and key European countries and initiating patients enrolment



Primary endpoint

- Change from baseline in ADCS-ADL score at week 24, and
- Change from baseline in ADAS-Cog 11 score at week 24

Main secondary endpoints

- Time to severe dementia (MMSE<10)
- Change from baseline in ADCS-ADL and ADAS-Cog score at week 48

Main inclusion criteria:

- Patient with clinical diagnosis of Alzheimer's disease based on cognitive impairment and daily functional dependency at screening visit
- Patients with ADCS-ADL score at screening visit and baseline visit < 73
- Patient with MMSE ≥ 14 and ≤ 25 at screening visit and baseline visit

Randomization

- 600 patients
- Randomization 1:1

Extension at week 48

- In case of an individual positive benefit-risk assessed by the investigator

Alzheimer's disease

Alzheimer's treatment are predominantly antibodies targeting amyloid plaques for the treatment of early Alzheimer's disease

Indications	Drug	MMSE *(Severity)* + -	Reduction in clinical decline		
			ADAS-Cog*	ADCS-ADL**	CDR-SB
Mild Moderate Alzheimer	**Masitinib**	**[14-25]**	**77%**	**71%**	**NA**
Early Alzheimer	**Aducanumab (Biogen)**	**[20 – 28]**	**27%** **11%**	**40%** **18%**	**22%** **-2%**
	Lecanemab (Esai Biogen)	**[22 – 30]**	**NA**	**NA**	**27%**
	Donanemab (Eli Lilly)	**[20 – 28]**	**≈40%**	**≈22%**	**NA**
	Crenezumab (Roche)	**≥22**	Stopped for futility		

Differentiating factors

Masitinib
- Oral treatment
- Targets mast cells & microglia

Antibodies
- IV treatment
- Targets amyloid plaques
- Negative efficacy outcome with Crenezumab
- Controversy with Aducanumab efficacy results
- Three deaths with lecanemab due brain swelling, bleeding, and seizures

* Different versions of the ADAS-Cog instrument used, over different timescales - for masitinib it was ADAS-Cog(11) at W48; for the Aduhelm studies it was ADAS-Cog(13) at W78.
** Different versions of the ADCS-ADL instrument used and over different timescales - for masitinib it was ADCS-ADL at W48; for the Aduhelm studies it was ADCS-ADL-MCI at W78.

Masitinib clinical program outside of neurology

Advanced pipeline in oncology and inflammatory diseases can add value to the neurology plateform

Therapeutic area	Indication	Results	Development Status
Inflammatory diseases	**Indolent systemic mastocytosis**	▪ First phase 3 completed (135 patients) ▪ Significant reduction in symptoms (pruritus, flushes, depression, asthenia)	▪ Confirmatory phase 3 on-going
	Mast cell activation syndrome (MCAS)	▪ None	▪ Phase 2 study on-going
	Severe asthma uncontrolled with OCS	▪ First phase 3 completed (419 patients) ▪ Significant decreases in asthma exacerbations regardless of eosinophil level	▪ Confirmatory phase 3 to be initiated
	Severe asthma uncontrolled with ICS	▪ First phase 3 completed (347 patients) ▪ Significant decreases in asthma exacerbations and improved quality of life	▪ Confirmatory phase 3 to be initiated
Oncology	**Metastatic castrate refractory prostate cancer**	▪ First phase 3 completed (580 patients) ▪ Significant increase in PFS in the pre-specified targeted subgroup (patients with ALP ≤ 250 IU/ml)	▪ Confirmatory phase 3 to be initiated
	Locally advanced pancreatic cancer with pain	▪ First phase 3 completed (383 patients) ▪ Significant OS increase in population with locally advanced tumors	▪ Confirmatory phase 3 to be initiated
Viral diseases	**Covid-19**	▪ Two phase 2 studies ongoing	▪ Status pending results from phases 2

Mastocytosis

Phase 3 demonstrated a significant reduction in symptoms with masitinib at 6.0 mg/kg/day

3.6 fold improvement in most prevalent symptoms

		Masitinib	Placebo	p-value	Odds ratio
Primary Analysis	**4H75% pruritus, flushes, depression, asthenia**	18.7%	7.4%	0.0076	**3.63**
Secondary Analyses	**3H75% pruritus, flushes, depression**	24.7%	9.8%	0.0071	**3.06**
	2H75% pruritus or flushes	27.2%	10.7%	0.038	**2.63**
	Pruritus 75% pruritus	22.0%	7.3%	0.032	**3.13**

Improvement in objective markers of the disease

	Masitinib	Placebo	p-value
Tryptase - Patients with baseline tryptase ≥20 µg/L	46	44	0.0001
Average relative change from baseline Mean±SD	-18.0 ± 21.4	2.2 ± 26.9	
Urticaria Pigmentosa (UP) - Patients with baseline UP	33	36	0.0210
Average relative change from baseline in the Body Surface Area (BSA) covered by UP (Wallace correction)	-12.34 ± 26.41	15.91 ± 59.79	
Darier's sign – Number of patients (baseline)	37	37	0.0187
Response rate for Darier's sign disappearance (Yes/No) in patients with "Darier's sign" at baseline	18.92%	2.70%	

Cumulative response based on the generalized estimating equation model with missing data considered as failure. Longitudinal analysis with respect to symptoms as opposed to patient response rate at a single point in time.
Response rates expressed as ratio of sum of actual responses between weeks 8 and 24 divided by the total number of possible responses over the same treatment period.
Respose = 75% reduction from baseline in symptoms severity
4H75% = cumulative response in severe symptoms present at baseline among the four :pruritus, flushes, depression, asthenia.
3H75% = cumulative response in severe symptoms present at baseline among the three: pruritus, flushes, depression.
2H75% = cumulative response in severe symptoms present at baseline among the two: pruritus, flushes.
NOTE that in *Lancet* article these endpoints use the nomenclature 4R75% etc, R standing for 'response', a term preferred over 'Handicap'.

Mastocytosis

Results from phase 3 were published in *The Lancet*

Masitinib for treatment of severely symptomatic indolent systemic mastocytosis: a randomised, placebo-controlled, phase 3 study

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Summary

Background Indolent systemic mastocytosis, including the subvariant of smouldering systemic mastocytosis, is a lifelong condition associated with reduced quality of life. Masitinib inhibits KIT and LYN kinases that are involved in indolent systemic mastocytosis pathogenesis. We aimed to assess safety and efficacy of masitinib versus placebo in severely symptomatic patients who were unresponsive to optimal symptomatic treatments.

Methods In this randomised, double-blind, placebo-controlled, phase 3 study, we enrolled adults (aged 18–75 years) with indolent or smouldering systemic mastocytosis, according to WHO classification or documented mastocytosis based on histological criteria, at 50 centres in 15 countries. We excluded patients with cutaneous or non-severe systemic mastocytosis after a protocol amendment. Patients were centrally randomised (1:1) to receive either oral masitinib (6 mg/kg per day over 24 weeks with possible extension) or matched placebo with minimisation according to severe symptoms. The primary endpoint was cumulative response (≥75% improvement from baseline within weeks 8–24) in at least one severe baseline symptom from the following: pruritus score of 9 or more, eight or more flushes per week, Hamilton Rating Scale for Depression of 19 or more, or Fatigue Impact Scale of 75 or more. We assessed treatment effect using repeated measures methodology for rare diseases via the generalised estimating equation model in a modified intention-to-treat population, including all participants assigned to treatment minus those who withdrew due to a non-treatment-related cause. We assessed safety in all patients who received at least one dose of study drug. This trial is registered with ClinicalTrials.gov, number NCT00814073.

Findings Between Feb 19, 2009, and July 15, 2015, 135 patients were randomly assigned to masitinib (n=71) or placebo (n=64). By 24 weeks, masitinib was associated with a cumulative response of 18·7% in the primary endpoint (122·6 responses of 656·5 possible responses [weighted generalised estimating equation]) compared with 7·4% for placebo (48·9 of 656·5; difference 11·3%; odds ratio 3·6; 95% CI 1·2–10·8; p=0·0076). Frequent severe adverse events (>4% difference from placebo) were diarrhoea (eight [11%] of 70 in the masitinib group *vs* one [2%] of 63 in the placebo group), rash (four [6%] *vs* none), and asthenia (four [6%] *vs* one [2%]). The most frequent serious adverse events were diarrhoea (three patients [4%] *vs* one [2%]) and urticaria (two [3%] *vs* none), and no life-threatening toxicities occurred. One patient in the placebo group died (unrelated to study treatment).

Interpretation These study findings indicate that masitinib is an effective and well tolerated agent for the treatment of severely symptomatic indolent or smouldering systemic mastocytosis.

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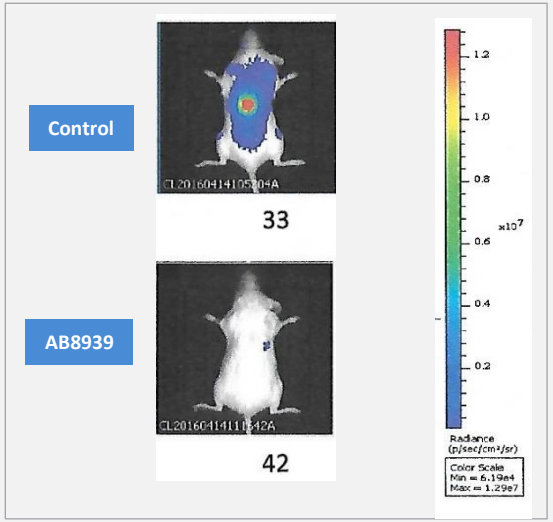
AB8939

AB8939 is a novel Microtubule-destabilizing drug able to cure mice with patient derived xenograft of Acute megakaryoblastic leukemia

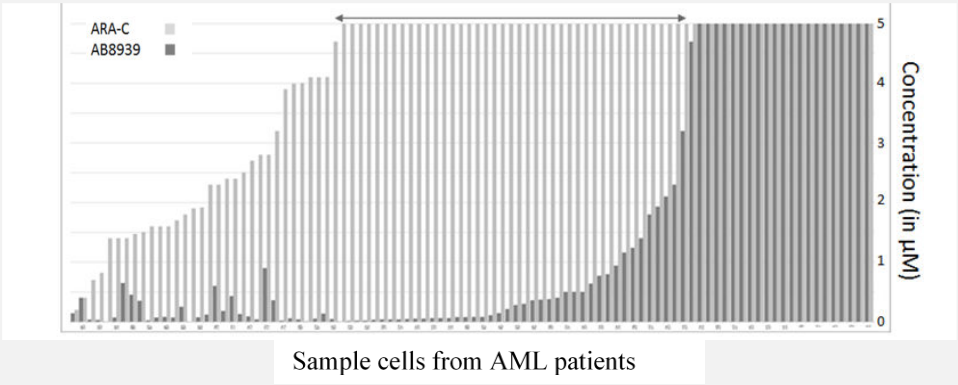
Key Differentiating factors

- Overcomes P-glycoprotein (Pgp) and myeloperoxidase (MPO) mediated resistance
- Active in Ara-C resistant/refractory AML
- Activity seen across all AML subtypes
- Alone or combined with Ara-C, improved survival and reduced disease burden relative to Ara-C
- Active in azacitidine resistant AML, with greatly reduced hematotoxicity
- Drug profile support development of AB8939 as a treatment of relapsed/refractory AML patients unable to receive intensive chemotherapy

Detection of AMKL26 PDX blasts in mice following single agent AB8939 treatment

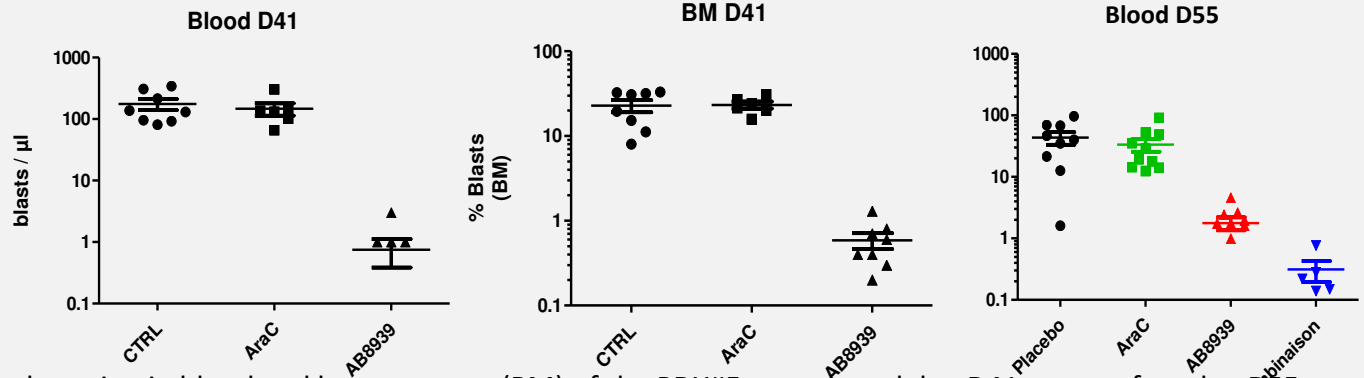


Activity of AB8939 in Ara-C resistant/refractory AML patent blasts



In proliferation assays, 66% of Ara-C-resistant blasts were sensitive to AB8939 and overall 69% of blasts had nanomolar sensitivity ($IC_{50} \leq 500$ nM)

Activity in Ara-C resistant PDX model



Blasts detection in blood and bone marrow (BM) of the PDX#5 mouse model at D41 post graft and at D55 post graft

AB8939

Phase 1/2 in refractory Acute Myeloid Leukemia is authorized by FDA and key European countries and actively enrolling patients

Phase 1/2 design

Design: Open-label, Uncontrolled, Multiple Doses, phase 1 study

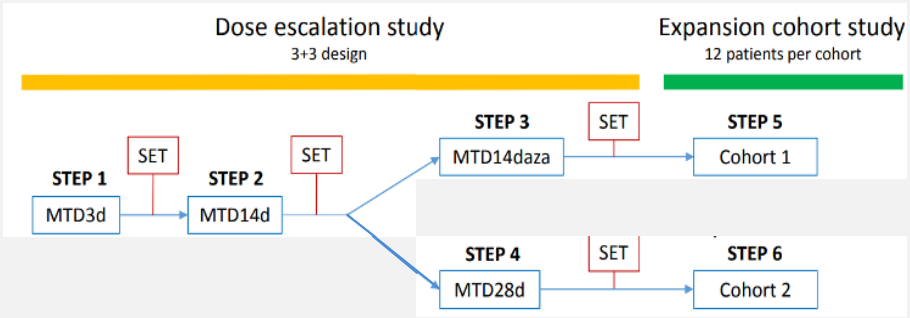
Main inclusion criteria:

- Patients with documented diagnosis of AML
- Patients in 2nd or 3rd line of treatment (if eligible in 1st line to high dose chemotherapy) OR in 2nd line of treatment (if not not eligible to high dose chemotherapy)
- Patients with refractory melyodisplastic syndrome in 2nd or 3rd line of treatment
- Patients not eligible to hematopoietic stem cell transplantation (HSCT) at the time of inclusion

Enrolment: 72 patients

Duration: 3 days, 14 days, and 28 days

Phase 1/2 Objectives



Phase 1 : Dose escalation

- Identify Maximum Tolerated Dose (MTD) at day 3, 14, and 28
- Identify Maximum Tolerated Dose (MTD) at day 14 in combination with azacitidine
- Determine the pharmacokinetics profile
- Recommend dose of expansion cohort

Phase 2 : Expansion cohort

- Determine early efficacy

Licensing

An investment bank has been mandated to seek potential licensing options for masitinib

Scope

- Clinical development and/or commercialization of masitinib
- In one indication, or neurology, or all indications
- In one key country, or one region, or all countries

Opportunity

- Advanced program in neurology
- Authorized by FDA and key European countries
- Rarity of late stage drugs belonging to small pharma
- Necessity to partner for commercialization
- Can sped-up clinical development

Potential discussions remain confidential

European Investment Bank (EIB)

AB Science is backed up by EIB, an institutional financial partner, with 15M€ long term debt secured and 30M€ under negotiation

Loan 1
15M€
(signed)

- Scope: Covid-19
- 3 tranches:
  - Tranche 1 (6M€) : Drawdown performed in December 2022
  - Tranche 2 (6M€) : Operational conditions already met
  - Tranche 3 (3M€) : Conditions of successful study and being referenced among potential Covid-19 treatment
- Differed interest payment
- 6 years maturity for Tranche 1, 5 years maturity for Tranche 2 and 3

Loan 2
30M€
(in negociation)

- Scope: Other indications developed with masitinib
- 3 tranches:
  - Tranche 1 (10M€) : Operational conditions already met
  - Tranche 2 (10M€) : Operational conditions will be met in the next 12 months
  - Tranche 3 (10M€) : Operational conditions will be met in the next 12 months
- Differed interest payment
- 6 years maturity for Tranche 1, 5 years maturity for Tranche 2 and 3