



AB SCIENCE WEBCONFERENCE

MASITINIB IN ALZHEIMER'S DISEASE

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Masitinib Profile and Mechanism of Action

Orally-administered kinase inhibitor selectively targeting mast cells and microglia

Masitinib targets mast cells

- Masitinib is a selective inhibitor of c-Kit, Lyn, and Fyn kinases
- These kinases play critical roles in the activation of mast cells

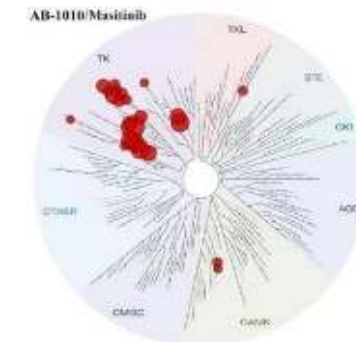
Masitinib targets macrophages/microglia

- Masitinib is a potent and selective inhibitor of MCSFR-1
- This kinase plays critical roles in the modulation of microglia

Masitinib is a tablet

- Oral route
- Morning and evening

Kinase inhibition profile of masitinib			
Cellular Target	Molecular Target	IC ₅₀ [nM]	Kd [μM]
Mast cells	KIT wild-type (WT)	20	0.008
	FYN	240	0.14
	LYN	225	0.061
Microglia	MCSFR-1	90	0.0076



Scientific Rationale in Alzheimer's disease (AD)

The mode of action of masitinib in AD is based on four targets, which may have a synergistic effect

Modulation of Microglia

- Microglia is involved in the neuro-inflammation in AD
- Masitinib blocks microglia through inhibition of MCSFR-1 kinase

Protection of Synapses

- Synapses are altered in AD
- Masitinib promotes recovery of synaptic markers in mice model of AD

Inhibition of Tau protein

- Tau protein aggregates in the physiopathology of AD
- Masitinib inhibits FYN kinase, a kinase that is phosphorylating Tau
- Masitinib prevent the accumulation of amyloid fibrill in hippocampus of young mice model of AD

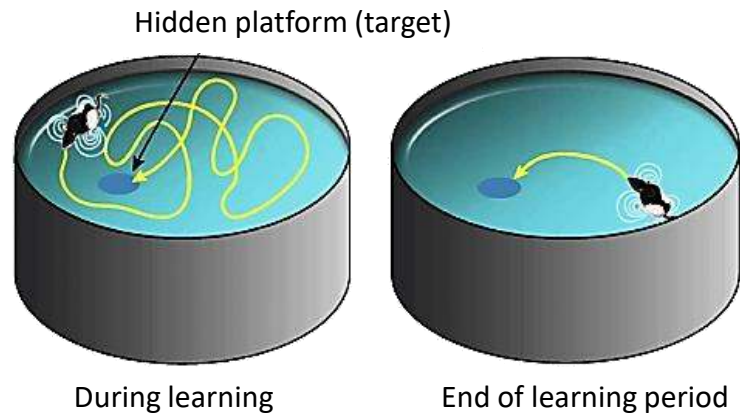
Control of Mast Cell (MCs) activity

- Mice depleted from MCs do not develop symptoms of AD
- Masitinib blocks MCs activation through inhibition of c-Kit, LYN, and FYN kinases
- β eta-amyloid plaques activate mast cells
- Transgenic AD mice treated by masitinib are protected for cognition impairment

Pharmacology

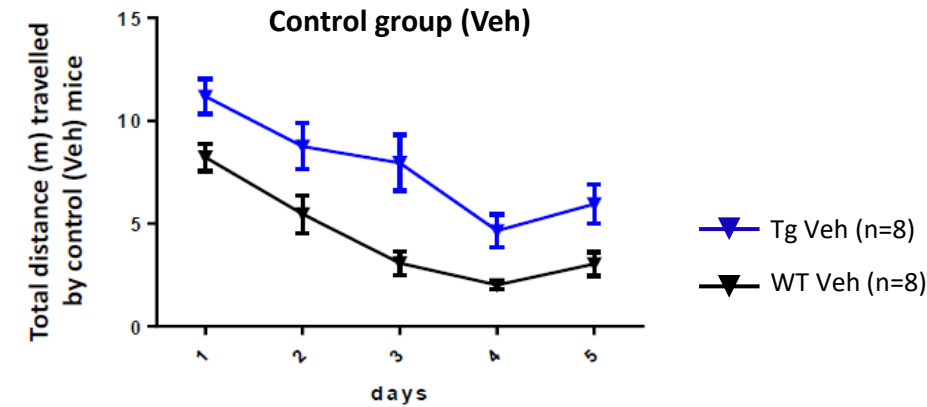
In a transgenic mouse model of AD, masitinib could restore/protect completely cognitive impairment

Cognitive evaluation in a curative setting (APPXPS1DE9 mouse model)

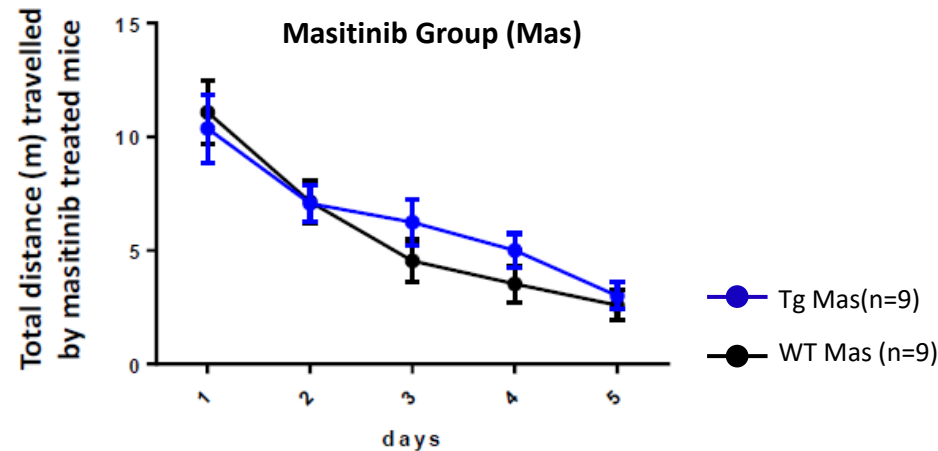


- ❖ Blinded study
- ❖ Masitinib was evaluated for its effect on memory deficit in AD mice (Tg) versus using the Morris Water Maze (MWM) in a curative setting (mice aged 12-14 months)
- ❖ The MWM test evaluates hippocampal-dependent learning, including acquisition of spatial memory and long-term spatial memory, which is often affected in AD.

Morris Water Maze (MWM) – Improvement in Acquisition Phase



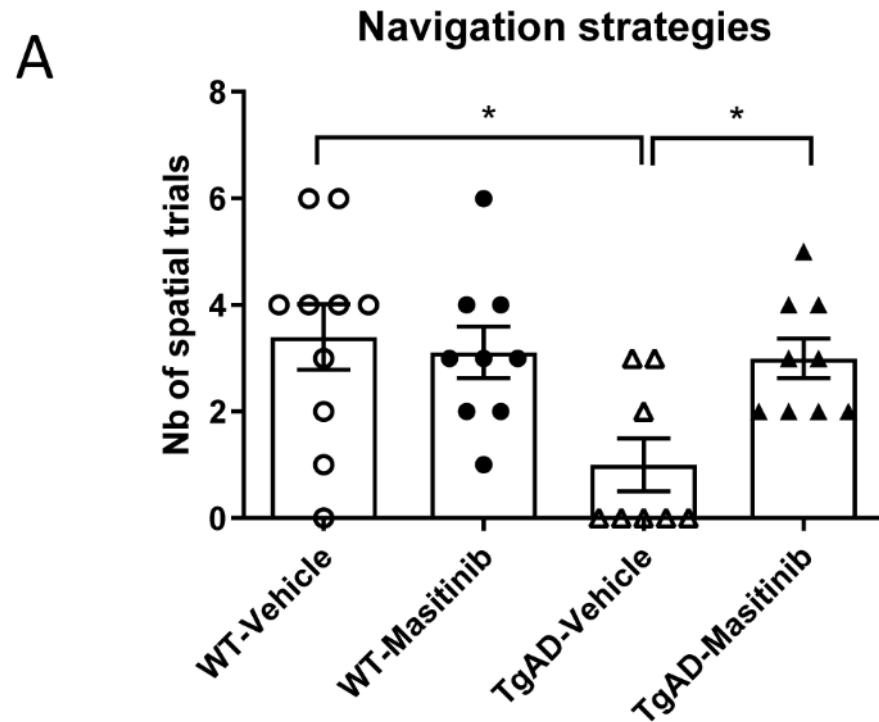
AD mice (Tg) have longer distance and no spatial memory improvement as compared with control mice (WT=wild-type)



AD mice (Tg) treated with masitinib improve cognitive function, with spatial memory returning to normal levels

In a transgenic mouse model of AD, masitinib could completely protect/restore the ability to perform navigation strategy

Morris Water Maze (MWM) – Improvement in Spatial Strategy



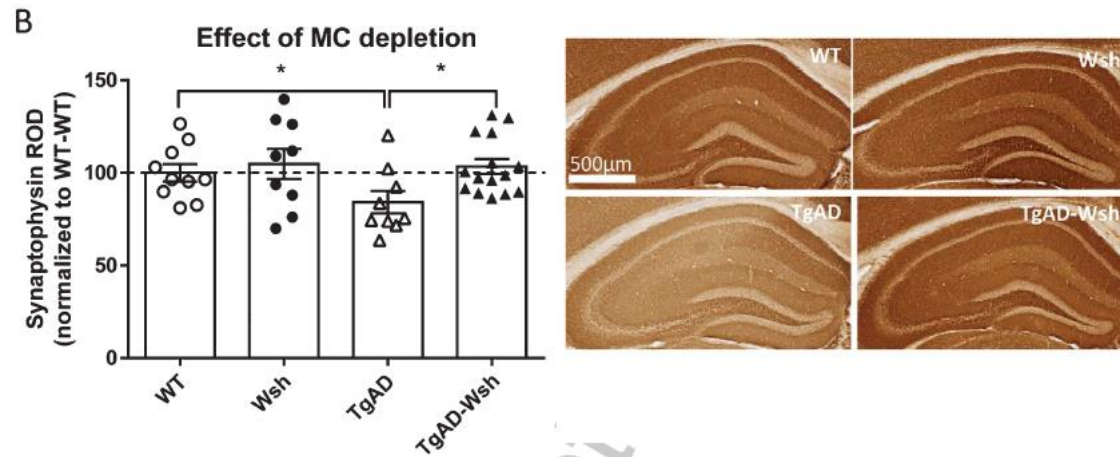
Group	p-value	Test
Tg Veh vs. Tg M	0.034	Treatment effect

* p<0.05. WT = wild-type mice. Tg = APPxPS1dE9 mice. M = masitinib treatment. Veh = vehicle treatment.

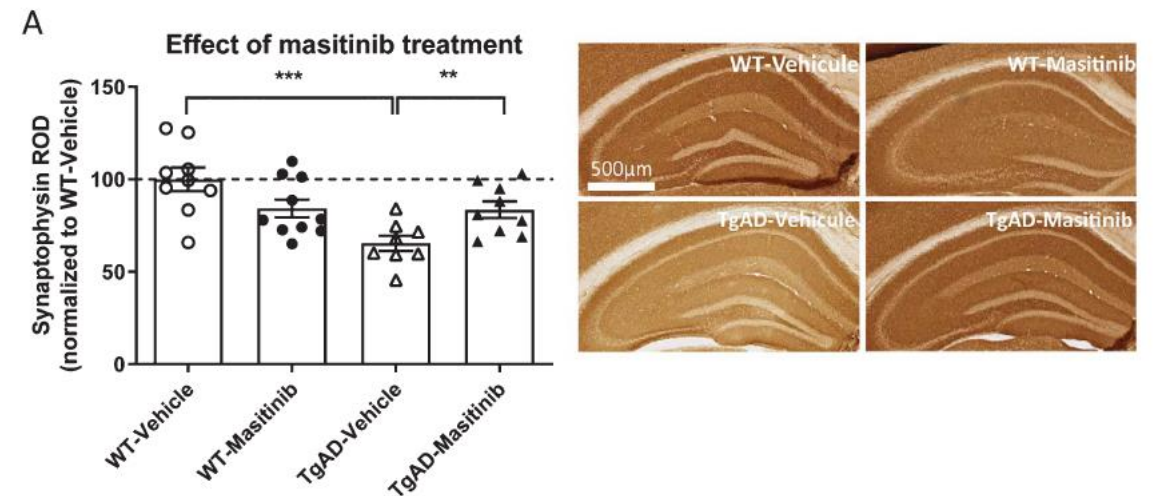
Pharmacology

In a transgenic mouse model of AD, masitinib could protect through mast cell inhibition against synaptic loss/destruction

Mast cell-deficient transgenic AD mice show a recovery of synaptic markers



Likewise, masitinib induces a recovery of synaptic markers in transgenic mice model of AD



WT = Wild-type mice. Wsh = Wild-type mice depleted in mast cells. TgAD = mice model of AD. TgAD-Wsh = mice model of AD depleted in mast cells. Veh = Vehicle

B. Relative optical density of synaptophysin immunoreactivity in the hippocampus of WT and TgAD mice with or without mast cells depletion induced by the Wsh mutation (left part) and representative microphotographs illustrating synaptophysin immunoreactivity levels in the four studied groups (right part).

A. Relative optical density of synaptophysin immunoreactivity in the hippocampus of WT and TgAD mice treated with Vehicle or masitinib (left part) and representative microphotographs illustrating synaptophysin immunoreactivity levels in the four studied groups (right part).

Data expressed as mean±SEM. ***p < 0.0001, **p < 0.01, *p < 0.05.

Masitinib Clinical Development Plan in AD

The development program in Alzheimer’s disease is comprised of AB04024 proof of concept study (*published*), and AB09004 phase 2B/3 study

Phase	Study code	Design	Population	Primary endpoint	Patient target	Related publications
2a	AB04024 (NCT00976118)	Double-blind, placebo-controlled, parallel-group study	Patients with mild to moderate Alzheimer Disease	Change on ADAS-Cog	34	Piette, 2011
2B/3	AB09004 (NCT01872598)	Prospective, double-blind, placebo-controlled, parallel groups study	Patients with mild to moderate Alzheimer Disease	Change on ADCS-ADL or Change on ADAS-Cog	720	

Positioning in AD

Masitinib is positioned in patients with mild and moderate dementia, which is different from other compounds

Disease severity	MMSE Score (mini mental state examination)
Prodromal	> 25
Mild	[21 – 25]
Moderate	[12 – 20]
Severe	< 12

Aducanumab

Prodromal AD
> 22 / > 24

Masitinib

Mild & Moderate AD
[12 – 25]

Standard of care in AD

There are currently four drugs used in the treatment of mild and moderate AD and approved 20 years ago

Year of approval	Drug	Class
1996	Donepezil	Cholinesterase inhibitors
2000	Rivastigmine	Cholinesterase inhibitors
2001	Galantamine	Cholinesterase inhibitors
2003	Memantine	NMDA Antagonist

Masitinib is used in add-on to Standard of Care

Primary clinical endpoints

Evaluation of efficacy is based on two clinical endpoints

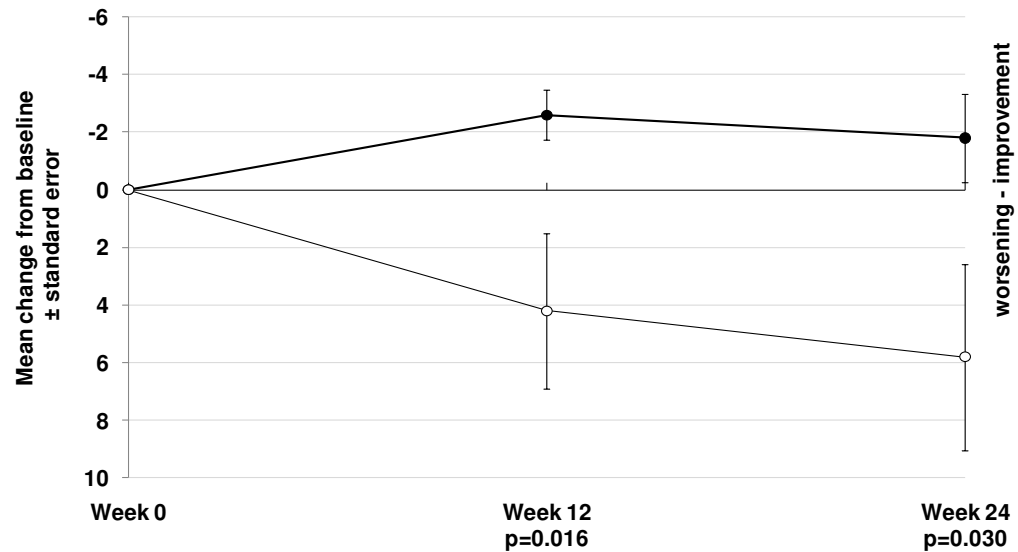
Clinical endpoint	Objective	Assessment	Measurement	Outcome
ADAS-Cog	Measure the effect on cognition and memory	By patient	11 Questions Maximum 70 points	The lower the better
ADCS-ADL	Measure self-care and activities of daily living	By caregiver	23 Questions Maximum 70 Points	The higher the better

AB04024 study results in Alzheimer's disease

A proof of concept study was published in 2011

Positive effect detected on cognitive function

Change in ADAS-Cog



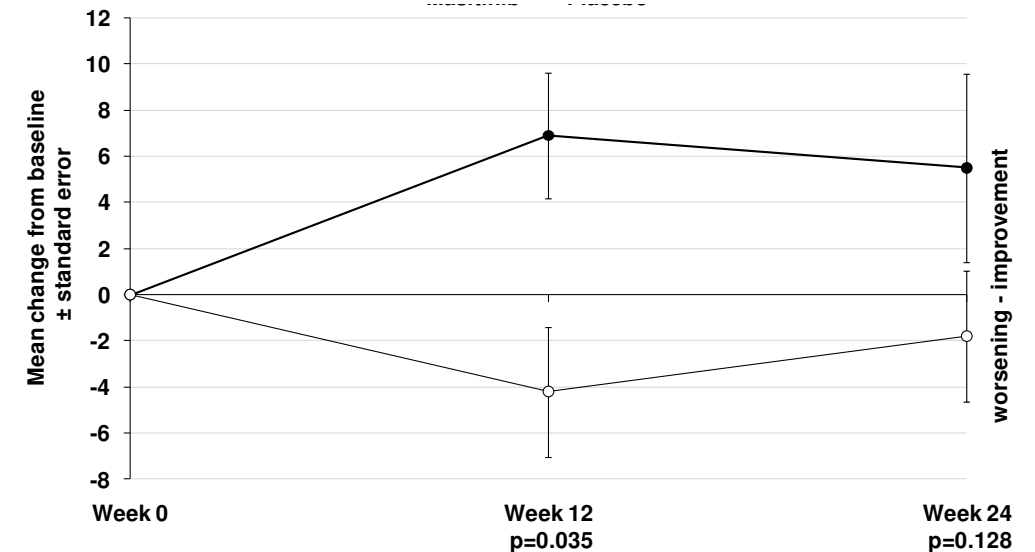
Phase 2a (n=34)

- Masitinib
- Placebo

Piette et al., *Alzheimers Res Ther.* 2011 Apr 19;3(2):16. doi: 10.1186/alzrt75.

Positive effect detected on Daily activity

Change in ADCS-ADL



AB09004 – Study Design

Study AB09004 evaluated, in add-on to standard of care, three doses of masitinib, each dose having its own placebo control

Design

Design:

Double-blind, Placebo-controlled, Randomized, Parallel-group Phase 3 Study to Evaluate the Safety and Efficacy of Masitinib in Patients With Mild to Moderate Alzheimer's Disease (AD), in add-on to Standard of Care

Standard of Care (SoC): Cholinesterase inhibitors, memantine

Doses tested:

- Masitinib 3 mg/kg/day (stopped early based on IDMC recommendation)
- Masitinib 4.5 mg/kg/day, randomisation 1:1
- Masitinib titration 4.5 to 6.0 mg/kg/day, randomisation 2:1

Planned Enrolment: 720 patients

Primary endpoint:

- Change in the Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog)
- Change in the Alzheimer's Disease Cooperative Study Activities of Daily Living (ADCS-ADL)

Duration: 24 weeks

Main inclusion criteria

- 1) Patient with dementia of Alzheimer's type, according to the Diagnostic and Statistical Manual of Mental Disorders criteria (DSM-IV)
- 2) Patient with probable Alzheimer's disease according to the NINCDS-ADRDA criteria (National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association)
- 3) Patient with MMSE ≥ 12 and ≤ 25 at baseline
- 4) Patient treated for a minimum of 6 months with a stable dose of cholinesterase inhibitors and/or a stable dose of memantine, with no changes foreseen in therapy throughout the study.

AB09004 – Study Design

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

Statistical analysis:

- Statistical risk Alpha (chance finding) split between ADAS-COG (2.5%) and ADCS-ADL (2.5%).
- Study is successful if the treatment effect is established **in at least one of the two primary endpoints**

Stratification factors

- MMSE score at baseline
- Age at baseline
- ADCS-ADL total score at baseline
- ADAS-COG total score at baseline

Populations analysed

- Primary analysis : FAS (Full Analysis Set)

Type I error was controlled at interim by the Haybittle-Peto alpha spending method

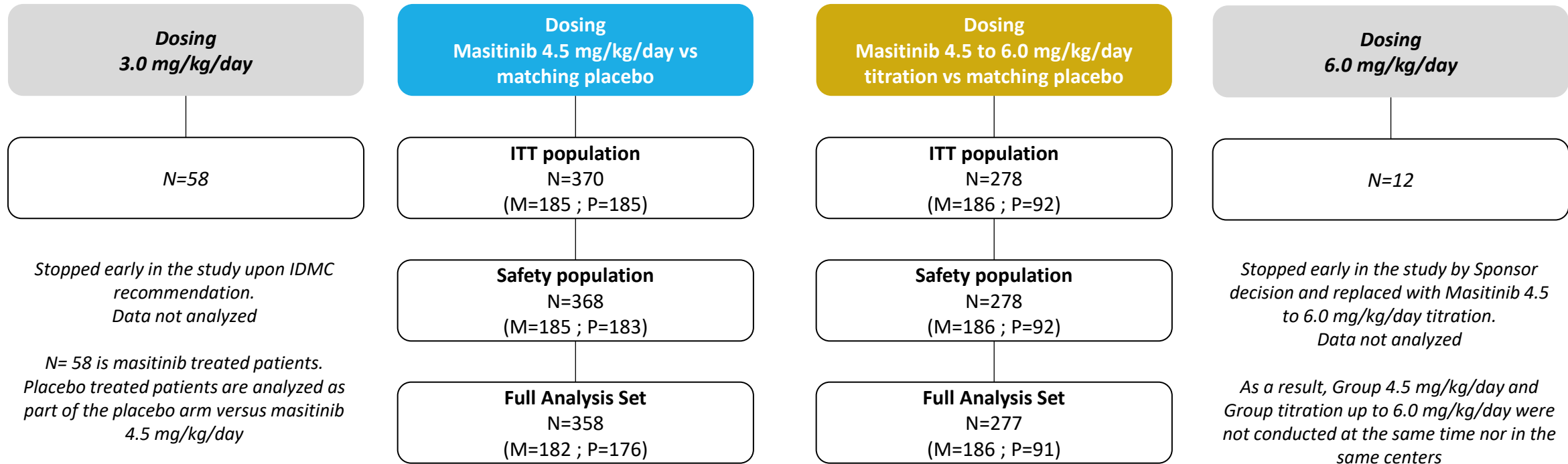
The efficacy criteria was tested at a significance level which defined as follows –

- Stop at interim and reject null hypothesis on primary endpoint if p-value < 0.001
- If at interim p-value > 0.001, continue to final analysis and efficacy criteria at final analysis is tested at 2.499% level for each of the primary endpoints

AB09004 – Population analyzed

The study was comprised of two independent sub-studies testing two distinct dosing regimens

Study AB09004 : N = 718 from 118 sites in 21 countries, 51.5% of patients enrolled in EU countries



Full Analysis Set : Exclusion from ITT population of 13 patients

- Patients from sites with critical GCP violations at 2 sites as highlighted by audit report and internal report (n=6)
- Patients with no treatment intake (n=2)
- Patients with baseline Adl or Cog scores that do not correspond to the medical history, with documented letter from investigator to exclude them from primary analysis, validated by steering committee (n=3)
- Patients with caregiver that changed during the main period, with documented letter from investigator to exclude them from primary analysis, validated by steering committee (n=2)

AB09004 – Baseline Characteristics

Baseline characteristics were balanced

Masitinib 4.5 mg/kg/day vs matching placebo

FAS	Masitinib + SoC (N = 182)	Placebo + SoC (N = 176)
Age (Years)		
Mean (std)	71.9 (8.28)	71.7 (8.21)
Median	73.0	73.0
>=50 - <60 [n (%)]	19 (10.4)	17 (9.4)
>=60 - <70 [n (%)]	44 (24.0)	52 (28.9)
>=70 - <80 [n (%)]	82 (44.8)	76 (42.2)
≥ 80 [n (%)]	38 (20.8)	35 (19.4)
Sex [n (%)]		
Female	114 (62.6)	98 (55.7)
MMSE		
12-20	119 (65.4)	115 (65.3)
21-25	63 (34.6)	61 (34.7)
Mean	18.8 (3.73)	18.6 (3.76)
Median	19.0	19.0
ADCS-ADL		
Mean (std)	51.8 (15.13)	51.4 (14.95)
Median	55.0	53.5
ADAS-COG		
Mean (std)	26.1 (10.13)	25.9 (9.67)
Median	25.5	24.8

Masitinib 4.5 to 6.0 mg/kg/day titration vs matching placebo

FAS	Masitinib + SoC (N = 186)	Placebo + SoC (N = 91)
Age (Years)		
Mean (std)	71.9 (8.29)	71.2 (8.11)
Median	72.0	72.0
>=50 - <60 [n (%)]	14 (7.5)	10 (11.0)
>=60 - <70 [n (%)]	54 (29.0)	26 (28.6)
>=70 - <80 [n (%)]	78 (41.9)	41 (45.1)
≥ 80 [n (%)]	40 (21.5)	14 (15.4)
Sex [n (%)]		
Female	118 (63.4)	57 (62.6)
MMSE		
12-20	123 (66.1)	57 (62.6)
21-25	63 (33.9)	34 (37.4)
Mean	18.8 (3.62)	18.7 (3.71)
Median	19.0	19.0
ADCS-ADL		
Mean (std)	52.4 (14.76)	53.2 (13.65)
Median	54.0	57.0
ADAS-COG		
Mean (std)	24.9 (10.08)	26.2 (10.64)
Median	24.3	24.3

AB09004 – Primary analysis - Cog - 4.5 mg/kg/day

The study met its primary analysis, demonstrating a statistically significant reduction in Cognitive impairment based on ADAS-COG (p=0.0003)

Significant effect on cognitive function after 24 weeks of treatment

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

Treatment	Descriptive Statistics		Model Summary - LSM		Difference		
	n	Mean (SD)	LS Mean	95% CI	LS Mean (SE)	97.51% CI	p-value
Masitinib 4.5 mg/kg/day + SoC	182	-1.51 (5.81)	-1.46	(-2.46, -0.45)	-2.15 (0.59)	(-3.48, -0.81)	0.0003
Placebo + SoC	176	0.63 (5.35)	0.69	(-0.36, 1.75)			

Imputation Model for missing Data

For the primary analysis, missing values are imputed by using the patient’s previous non-missing score and data from other similar patients (same cluster) that have continued treatment.

AB09004 – Cog J2R sensitivity analysis - 4.5 mg/kg/day

Cog sensitivity analysis based on Jump to reference imputation method remained positive, demonstrating a robust treatment effect

Significant effect on cognitive function confirmed based on Jump to Reference analysis

Change in ADAS-Cog - ANCOVA Analysis (Jump to Reference) - M4.5 vs Placebo

Treatment	Descriptive Statistics		Model Summary - LSM		Difference		
	n	Mean (SD)	LS Mean	95% CI	LS Mean (SE)	95% CI	p-value
Masitinib 4.5 mg/kg/day + SoC	182	-1.24 (5.86)	-1.04	(-2.06, -0.03)	-1.89 (0.60)	(-3.06, -0.72)	0.0016
Placebo + SoC	176	0.63 (5.35)	0.85	(-0.21, 1.91)			

The Jump to Reference (J2R) approach

The Jump to Reference, which is the most conservative approach, imputes the Placebo estimates for all patients who prematurely discontinued due to *lack of efficacy* and *toxicity* (related TEAE) in the treatment arm.

AB09004 – Adl - 4.5 mg/kg/day

The study demonstrated a statistically significant improvement on daily activity based on ADCS-ADL (p=0.0381)

Significant effect on daily activity after 24 weeks of treatment

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

Treatment	Descriptive Statistics		Model Summary - LSM		Difference		
	n	Mean (SD)	LS Mean	95% CI	LS Mean (SE)	97.51% CI	p-value
Masitinib 4.5 mg/kg/day + SoC	182	0.51 (7.78)	1.01	(-0.48, 2.50)	1.82 (0.87)	(-0.15, 3.79)	0.0381
Placebo + SoC	176	-1.09 (9.17)	-0.81	(-2.36, 0.74)			

Imputation Model for missing Data

For the primary analysis, missing values are imputed by using the patient’s previous non-missing score and data from other similar patients (same cluster) that have continued treatment.

AB09004 – Adl J2R sensitivity analysis - 4.5 mg/kg/day

Adl sensitivity analysis based on Jump to reference imputation method showed a numerical advantage close to statistical significance in favor of masitinib

Numerical advantage close to statistical significance on daily activity based on sensitivity analyses

Change in ADCS-Adl - ANCOVA Analysis (Jump to Reference) - M4.5 vs Placebo

Treatment	Descriptive Statistics		Model Summary - LSM		Difference		
	n	Mean (SD)	LS Mean	95% CI	LS Mean (SE)	95% CI	p-value
Masitinib 4.5 mg/kg/day + SoC	182	0.39 (7.79)	0.81 (0.76)	(-0.68, 2.30)	1.71 (0.87)	(-0.01, 3.43)	0.0512
Placebo + SoC	176	-1.09 (9.17)	-0.90 (0.79)	(-2.46, 0.65)			

The Jump to Reference (J2R) approach

The Jump to Reference, which is the most conservative approach, imputes the Placebo estimates for all patients who prematurely discontinued due to *lack of efficacy* and *toxicity* (related TEAE) in the treatment arm.

AB09004 – Cog and Adl analysis in mITT - 4.5 mg/kg/day

mITT analysis shows that the Cog analysis remained positive and Adl analysis lost statistical significance

Post-Hoc Analysis (ANCOVA) in mITT - M4.5 vs Placebo

Treatment	Descriptive Statistics		Model Summary - LSM		Difference		
	n	Mean (SD)	LS Mean	95% CI	LS Mean (SE)	95% CI	p-value
Change in ADAS-Cog							
Masitinib 4.5 mg/kg/day + SoC	183	-1.49 (5.81)	-1.45 (0.51)	(-2.45, -0.45)	-2.10 (0.59)	(-3.25, -0.95)	0.0004
Placebo + SoC	180	0.61 (5.30)	0.65 (0.53)	(-0.39, 1.69)			
Change in ADCS-Adl							
Masitinib 4.5 mg/kg/day + SoC	183	0.57 (7.79)	1.09 (0.76)	(-0.41, 2.59)	1.58 (0.88)	(-0.16, 3.31)	0.07426
Placebo + SoC	180	-0.76 (9.35)	-0.49 (0.79)	(-2.05, 1.08)			

mITT population :

- Exclude 8 patients from sites with critical GCP violations at 2 sites as highlighted by audit report and internal report (n=6) and with no treatment intake (n=2)
- Retain patients with baseline Adl or Cog scores that do not correspond to the medical history, with documented letter from investigator to exclude them from primary analysis, validated by steering committee (n=3), and patients with caregiver that changed during the main period, with documented letter from investigator to exclude them from primary analysis, validated by steering committee (n=2)

AB09004 – CIBIC - 4.5 mg/kg/day

The study demonstrated a 71% improvement on CIBIC as compared with placebo, statistically significant (p=0.040)

CIBIC (Improve) - Logistic Regression Analysis (Full Analysis Set) - M4.5 vs Placebo

Treatment	Descriptive Statistics	Count (percentage)		Statistic	
		Improvement	Worsening/No Change	OR (95% CI)	p-value
Masitinib 4.5 mg/kg/day + SoC	182	47 (25.82)	91 (50.00)	1.71 (1.02, 2.85)	0.0400
Placebo + SoC	176	36 (20.45)	119 (67.61)		

Modified Last Observation Carried Forward (mLOCF)

Comparison between treatment groups performed on the difference between improvement [1-3] and worsening [5-7] CIBIC-plus classes (improvement minus worsening) at Week 24 by using a chi square test for proportions comparison, using Modified Last Observation Carried Forward (mLOCF) methods for the management of missing data.

The mLOCF approach carries forward the last observed value for patients who prematurely discontinue due to *lack of efficacy* and *toxicity* (related TEAE).

AB09004 – MMSE / CDR / NPI - 4.5 mg/kg/day



The study showed a numerical advantage non statistically significant in favor of masitinib on MMSE, CDR, and NPI

Summary of change from baseline (mLOCF) of All Secondary Endpoints Over Time by Treatment - Full Analysis Set - M4.5 vs Placebo

Parameter	Treatment	Statistics	Week 8	Week 12	Week 24	
Mini-Mental State Examination (MMSE)	Masitinib + SoC	n	156	149	139	
		Mean (SD)	0.49 (2.67)	0.79 (2.89)	0.35 (3.04)	
	Placebo + SoC	n	170	163	155	
		Mean (SD)	0.09 (2.52)	0.66 (2.77)	0.22 (3.02)	
			Diff. of M-P	0.40	0.12	0.13
	Clinical Dementia Rating (CDR)	Masitinib + SoC	n	123	146	136
Mean (SD)			-0.05 (0.42)	-0.03 (0.41)	-0.01 (0.49)	
Placebo + SoC		n	116	162	155	
		Mean (SD)	-0.01 (0.41)	0.06 (0.48)	0.01 (0.55)	
			Diff. of M-P	-0.04	-0.09	-0.02
Caregiver Distress (NPI)		Masitinib + SoC	n	87	103	95
	Mean (SD)		-1.08 (3.58)	-0.50 (4.62)	0.61 (4.88)	
	Placebo + SoC	n	77	120	108	
		Mean (SD)	-0.66 (3.05)	-0.13 (3.73)	0.85 (4.64)	
			Diff. of M-P	-0.42	-0.38	-0.24
	Frequency and Severity (NPI)	Masitinib + SoC	n	87	103	95
Mean (SD)			-2.06 (7.51)	-0.72 (9.12)	1.18 (10.20)	
Placebo + SoC		n	77	120	108	
		Mean (SD)	-0.66 (5.58)	-0.11 (7.81)	2.19 (8.70)	
			Diff. of M-P	-1.40	-0.61	-1.01

AB09004 – Cog and Adl analysis – titration 6.0 mg/kg/day

No significant treatment-effect was observed either on Cog or Adl for high-dose masitinib (titration up to 6.0 mg/kg/day)

ANCOVA Analysis (Full Analysis Set) - M4.5 up to 6.0 vs Placebo

Treatment	Descriptive Statistics		Model Summary - LSM		Difference		
	n	Mean (SD)	LS Mean	95% CI	LS Mean (SE)	95% CI	p-value
Change in ADAS-Cog							
Masitinib 4.5 to 6.0 mg/kg/day + SoC	186	-0.54 (4.50)	-0.18 (0.47)	(-1.10, 0.73)	-0.43 (0.61)	(-1.81, 0.95)	0.4828
Placebo + SoC	91	-0.26 (5.46)	0.25 (0.60)	(-0.94, 1.43)			
Change in ADCS-Adl							
Masitinib 4.5 to 6.0 mg/kg/day + SoC	186	0.53 (6.15)	0.57 (0.62)	(-0.69, 1.80)	0.20 (0.82)	(-1.64, 2.04)	0.8073
Placebo + SoC	91	0.25 (6.98)	0.37 (0.81)	(-1.22, 1.96)			

Improvement under placebo possibly influenced by low number for placebo (n<100)

Improvement in mean Cog
(Mean = - 0.26)

Improvement in mean daily activity
(Mean = 0.25)

No higher efficacy with masitinib titration to 6.0 vs 4.5 mg/kg/day

Cognitive function
(Mean = - 0.54 with M6 vs -1.51 with M4.5)

Daily activity
(Mean = 0.53 with M6 vs 0.51 with M4.5)

We can conclude that the effective dose in Alzheimer’s disease for masitinib is 4.5 mg/kg/day

AB09004 – 4.5 mg/kg/day vs combined placebo

In order to assess the impact of the divergent placebo effect, masitinib 4.5 mg/kg/day was compared with the pooled placebo arms and Cog analysis remained significant

Significant effect on Cog with masitinib 4.5 versus combined placebo

ANCOVA Analysis (Full Analysis Set) - M4.5 vs Combined Placebo

Treatment	Descriptive Statistics		Model Summary - LSM		Difference		
	n	Mean	LS Mean	95% CI	LS Mean (SE)	95% CI	p-value
Change in ADAS-Cog							
Masitinib 4.5 mg/kg/day + SoC	182	-1.51 (5.81)	-1.16	(-2.12, -0.19)	-1.90 (0.53)	(-2.95, -0.85)	0.0004
Combined Placebo + SoC	267	0.33 (5.40)	0.74	(-0.15, 1.63)			
Change in ADCS-AdI							
Masitinib 4.5 mg/kg/day + SoC	182	0.51 (7.78)	1.00	(-0.39, 2.39)	1.33 (0.77)	(-0.18, 2.84)	0.0838
Combined Placebo + SoC	267	-0.64 (8.50)	-0.33	(-1.61, 0.95)			

AB09004 – Severe Dementia - 4.5 mg/kg/day vs combined placebo

There were significantly fewer patients reaching severe dementia stage (MMSE<10) and a significant decrease in time to severe dementia with masitinib 4.5 mg/kg/day compared with the pooled placebo arms

Significant effect on severe dementia (MMSE<10) with masitinib 4.5 versus combined placebo

Dementia- M4.5 vs Placebo Pooled (FAS)

Treatment group	Total	No. of Events	Percentage Events	No. Censored	Percentage censored	Median [95% CI]	p-value		Hazard	
							KM p-Value	Log Rank	Ratio (95% CI)	p-Value
Masitinib 4.5 mg/kg/ day	182	2	1.10	180	98.90	Not reached [;]	0.0446	0.0403	0.19 (0.0,0.8)	0.0276
Pooled Placebo	267	15	5.62	252	94.38	6.3 [5.9;6.3]				

Baseline MMSE (FAS)	Masitinib + SoC (N = 182)	Pooled Placebo + SoC (N =267)
< 14	18 (9.9)	30 (11.2)
< 17	54 (29.7)	81 (30.3)

AB09004 – Safety Overview



The safety of masitinib consistent with its known tolerability profile

Summary of Adverse Events – Safety population - [W0-W24] period

	Masitinib 3.0 + SoC (N = 58) n (%)	Masitinib 4.5 + SoC (N = 185) n (%)	Masitinib 4.5 to 6.0 + SoC (N = 186) n (%)	Placebo + SoC (N = 280) n (%)
At least one AE	53 (91.4)	161 (87.0)	160 (86.0)	217 (77.5)
At least one serious AE (non-fatal)	6 (10.3)	24 (13.0)	25 (13.4)	15 (5.4)
At least one severe AE	9 (15.5)	49 (26.5)	47 (25.3)	54 (19.3)

Among the 13% and 13.4% SAEs with masitinib (M4.5 and M6), 4.8% and 4.9 % were associated with mild or moderate adverse events, respectively

AB09004 – Safety Overview



The increase in Serious adverse events was equally distributed across all organ classes

Non - Fatal Serious Adverse Events by System Organ Class – Safety population - [W0-W24] period

	Masitinib 3.0 + SoC (N = 58) n (%)	Masitinib 4.5 + SoC (N = 185) n (%)	Masitinib 4.5 to 6.0 + SoC (N = 186) n (%)	Placebo + SoC (N = 280) n (%)
At least one Serious Adverse Event	6 (10.3)	24 (13.0)	25 (13.4)	15 (5.4)
Skin and subcutaneous tissue disorders	1 (1.7)	3 (1.6)	9 (4.8)	0 (0.0)
Infections and infestations	0 (0.0)	6 (3.2)	3 (1.6)	3 (1.1)
Blood and lymphatic system disorders	3 (5.2)	4 (2.2)	4 (2.2)	0 (0.0)
Gastrointestinal disorders	0 (0.0)	4 (2.2)	1 (0.5)	1 (0.4)
Neoplasms benign, malignant and unspecified	0 (0.0)	3 (1.6)	1 (0.5)	2 (0.7)
Cardiac disorders	0 (0.0)	4 (2.2)	1 (0.5)	0 (0.0)
Injury, poisoning and procedural complications	0 (0.0)	0 (0.0)	0 (0.0)	5 (1.8)
Investigations	1 (1.7)	1 (0.5)	2 (1.1)	1 (0.4)
Hepatobiliary disorders	0 (0.0)	1 (0.5)	1 (0.5)	2 (0.7)
Nervous system disorders	1 (1.7)	1 (0.5)	2 (1.1)	0 (0.0)
General disorders and administration site conditions	0 (0.0)	0 (0.0)	3 (1.6)	0 (0.0)
Renal and urinary disorders	0 (0.0)	3 (1.6)	0 (0.0)	0 (0.0)
Respiratory, thoracic and mediastinal disorders	0 (0.0)	2 (1.1)	1 (0.5)	0 (0.0)
Immune system disorders	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)
Metabolism and nutrition disorders	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Musculoskeletal and connective tissue disorders	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Reproductive system and breast disorders	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)

Intellectual Property

A new patent was filed based on results from study AB09004, which would permit AB Science to retain exclusive rights on the use of masitinib in Alzheimer’s disease until 2041.

Protection	Item	Duration of protection	Status
Patent on composition of matter and PTE	Patent on composition of matter has been filed and delivered. It will be further extended until 2028 through patent term extension (PTE)	Until 2028	Delivered
Synthesis process patent	A further protection until 2028 has been achieved through synthesis ‘process’ patent	Until 2028	Delivered
Phase 2/3 ‘Method of use’ patents	New patent based on results from study AB09004	Until 2041	Filed

Market potential

Indication	Prevalence
Alzheimer's Disease	1,000 / 100,000 ¹
Mild and moderate forms of Alzheimer's Disease*	60% ²

Estimated number of potential eligible patients	
US Patients	EU Patients
2,000,000	3,000,000

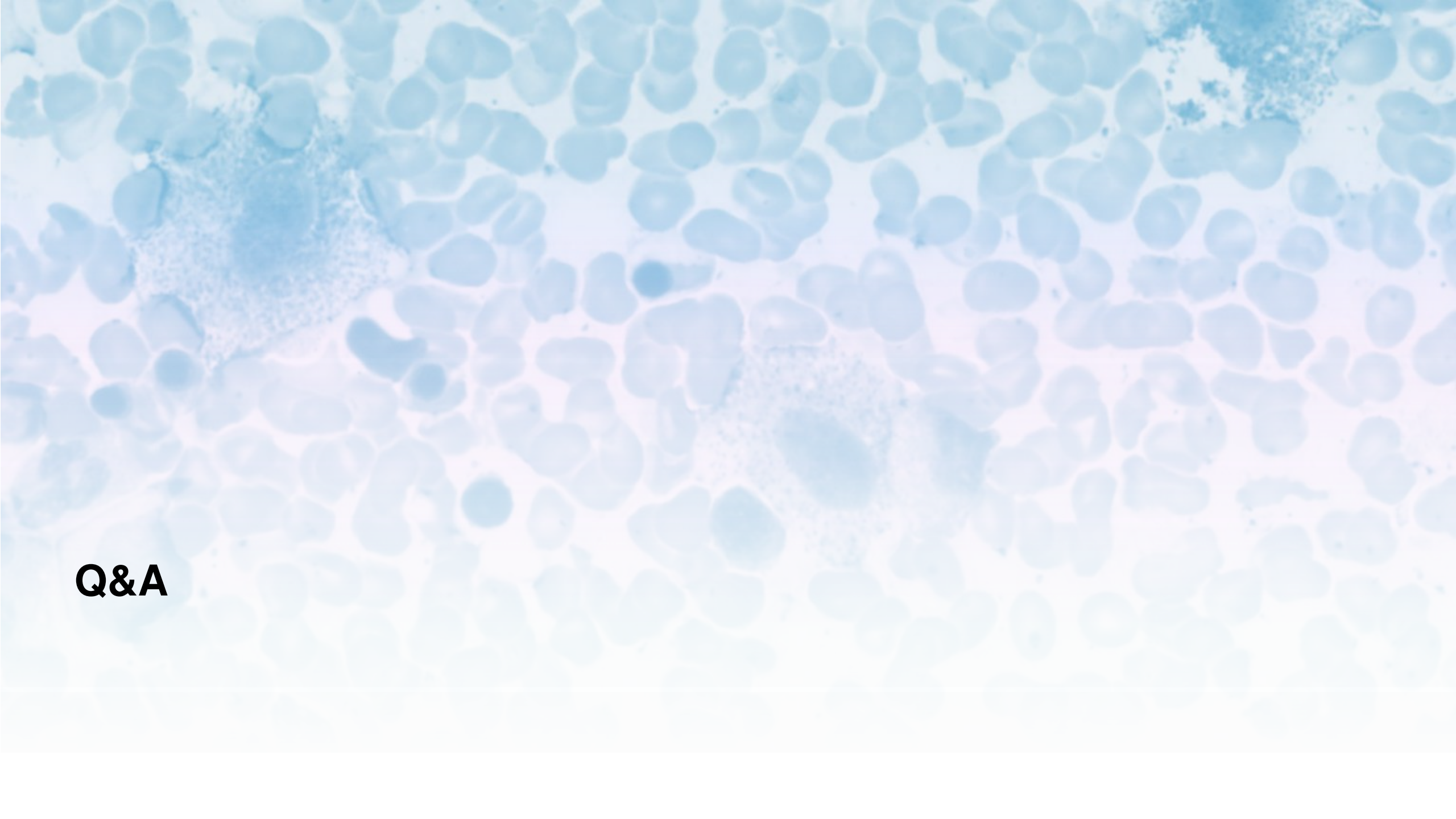
Annual cost of drugs registered in the indication
No approved drug as an add-on to cholinesterase inhibitors or memantine

* : expressed as percentage of Alzheimer's Disease

Source :

Population : <https://data.worldbank.org/indicator/SP.POP.TOTL> and <https://ec.europa.eu/eurostat/web/population-demography-migration-projections/population-data/main-tables>

1. Weili Xu et al. Epidemiology of Alzheimer's Disease. 2013.doi: 10.5772/54398
2. <https://www.j-alz.com/editors-blog/posts/when-do-we-diagnose-severe-alzheimers-disease>



Q&A