Safety, tolerability and immunogenicity of an active anti-Aβ40 vaccine (ABvac40) in patients with amnestic mild cognitive impairment (a-MCI) or very mild Alzheimer's Disease (Vm-AD): a randomized, double-blind, placebo-controlled, phase II trial.

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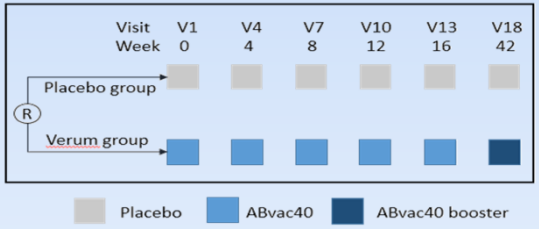
BACKGROUND

Alzheimer's disease is one of the biggest burdens of society with a dramatic and growing worldwide incidence rate. Notwithstanding scientific and medical advances, the condition remains incurable. Immunotherapies intended to act on the amyloid cascade are currently among the most hopefully disease modifying approaches. Aβ40 is in the core of the amyloid plaques and is the main component of vascular amyloid deposition which is associated with earlier dementia onset in AD. These data further the hypothesis that it should be targeted in treatment strategies. Araclon Biotech is developing an active vaccine directed specifically against the Aβ-40 peptide.

METHODS

This is a phase II, double-blind, randomized, placebo- controlled study in patients with amnestic mild cognitive impairment (a-MCI) or very mild Alzheimer's Disease (Vm-AD). The study will last for 104 weeks (from V0 to V25) during which the patients will receive five monthly (every four weeks) immunizations plus a booster shot. The primary objective of this trial is to confirm the safety, tolerability and immunogenicity results obtained in phase I and to explore the effect of the treatment on disease biomarkers (neuroimaging, CSF and plasma) and cognition as secondary efficacy variables.

STUDY DESIGN



PRELIMINARY RESULTS

1. Demographics and Baseline Characteristics

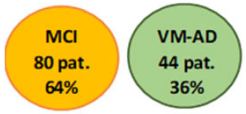
Table 1: Demographics

	Safety population (N=124)
Age	
Mean (SD)	70.4 (5.7)
Level of education	
Some school	41 (33.1)
High school graduate	37 (29.8%)
College graduate	11 (8.9%)
University degree	35 (28.2%)
Gender	
Male	50 (40,3%)
Female	74 (59.7%)
Time from diagnosis (mo)	
Mean (SD)	12.9 (11.7)
Race n(%)	
Caucasian	118 (98.3%)
Other	2 (1.7%)
MMSE Screening	
Mean (SD)	25.9 (1.8)
RBANS Screening	
Mean (SD)	67.2 (11.2)

Baseline demographics and clinical characteristics of all patients included in the safety analysis set.

Figure 1: Baseline amyloid–PET status

Figure 2: Baseline Diagnosis



2. Actual Status and Patient's population description

Table 2: Actual Status

	# Patients
Screened	238
Screening Failure	103 (43%)
NPS Status	49 (21%)
MRI	18 (8%)
Blood test	18 (8%)
EKG	3 (1%)
Other	15 (6%)
Randomized	135 (57%)
Dosed	124 (52%)
Discontinued	8 (6%)
SAE not related	3 (37%)
PI decision	1 (13%)
Consent withdrawal	4 (50%)

Patients (between 55-80 years of age) diagnosed either with a-MCI or vm-AD will be included in the trial. To ensure the primary safety and efficacy endpoints of the study a minimum of 60 subjects with a-MCI or vm-AD per treatment group (verum and placebo) are required. The amyloid-PET positive and amyloid-PET negative patients will be independently randomized following a ratio 1:1 between verum and placebo.

3. Safety and tolerability of ABvac40

Safety analysis population was defined as patients having at least one administration of ABvac40/placebo. As June 2020, a total of 124 patients are in safety population.

Table 3: Total AEs occurring

	Safety population (N=124)	
	# AEs	# Patients
Total of AEs	516	109 (88.00%)
Nervous system disorders	64	10 (32.0%)
Psychiatric disorders	12	11 (9.0%)
Cardiac disorders	9	8 (6.5%)
Vascular disorders	9	9 (7.0%)

Table 4: Summary of Treatment Emergent AE

	Safety population (N=124)	
	# AEs	# Patients
Total of AEs	516	109 (88.00%)
Treatment discontinuation	13	10 (8.1%)
Treatment -caused AE	148	48 (38.7%)
Serious AE	32	22 (17.7%)
Serious Treatment-caused AE	15	9 (7.3%)
Death	0	0 (0.0%)

Until now seventeen imaging findings have been reported. Fourteen was identified as microhemorrages initially reported as an amyloid-related imaging abnormalities (ARIA-H), one macro-haemorrage, one cerebral infarct and one siderosis. A 64% of these events were considered mild in severity.

Table 4: Imaging safety findings

	Safety population (N=124)	
	# AEs	# Patients
Total Serious AE	32	22 (17.7%)
Imaging safety findings (reported as a SAE according protocol)	18	11 (8.9%)
ARIA-H	14	10 (8.0%)
Macro-haemorrage	1	1 (0.8%)
Siderosis	1	1 (0.8%)
Infarct	1	1 (0.8%)
ARIA-E	1	1 (0.8%)

CONCLUSION

ABvac40 Phase II study is progressing as scheduled. Recruitment has been completed, first futility analysis has been passed. We are hopeful that the trial will meet the primary objectives regarding safety, tolerability and immune response.