UPDATE PHASE 2 STUDY OF ABVAC40, AN ACTIVE VACCINE ANTI-AB40 IN PATIENTS WITH MILD COGNITIVE IMPAIRMENT OR VERY-MILD ALZHEIMER'S DISEASE

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OBJECTIVES

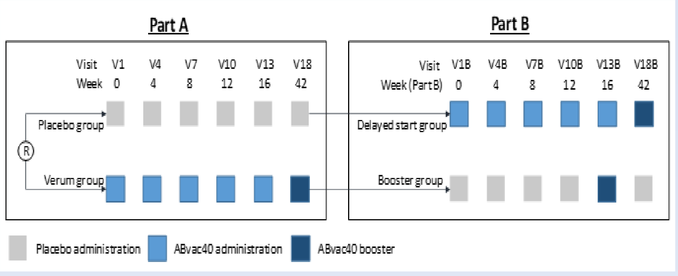
One of the main hallmarks of Alzheimer's disease (AD) is the deposition of amyloid-β peptides (Aβ) in the neuropil and blood vessels. Araclon Biotech is developing ABvac40, an active vaccine against Aβ40 peptide, one of the peptides present in senile plaques and the dominant peptide in vascular deposits, that has been associated with earlier onset of dementia. ABvac40 was designed to prevent the known risks of active immunization against amyloid peptides and eliciting an immune response, using a short C-terminal fragment of Aβ1-40 as immunogen that can only be recognized and bound to antibodies ones Aβ is cleaved and secreted. In a Phase 1 clinical trial (NCT03113812), ABvac40 showed to be safe and tolerable and generated a long-lasting antibody response (56 weeks) after only three-monthly immunizations (*Lacosta et al, Alzheimer's Research & Therapy 2018*).

The main objective of this poster is to present the **Top Line Data** of AbVAC40 placebo-controlled Phase 2 study in amnestic mild cognitive impairment (a-MCI) or very mild AD (vm-AD) patients.

METHODS

In 2017, Araclon Biotech initiated a Phase 2, 24-month, multicenter, randomized, double-blind, placebo-controlled trial in patients with a-MCI or vm-AD to investigate the safety, tolerability, and immune response of repeated subcutaneous injections of ABvac40 as well as explore the effect of treatment on biomarkers and cognition (Part A) (NCT03461276). Remarkably amyloid-PET negative patients were also included in the study (Fig. 1). In July 2020, a protocol amendment was approved whereby the blind phase (Part A) was shortened from 24 to 18-months and an additional 18-months cross-over study (Part B) was added.

STUDY DESIGN



TOP LINE DATA (Part A)

1. Demographics and baseline characteristics

Table 1: Demographics

		Abvac 40 (n= 62)	Placebo (n= 62)	P-value
Age	Mean (SD)	70.6 (6.0)	70.1 (5.5)	0.629
Education (%)				
	Some school	25 (40.3%)	16 (25.8%)	0.246
	High school graduate	15 (24.2%)	22 (35.5%)	
	College graduate	4 (6.5%)	7 (11.3%)	
	University degree	18 (29.0%)	17 (27.4%)	
Sex (%)				
	Male	24 (38.7%)	26 (41.9%)	0.714
	Female	38 (61.3%)	36 (58.1%)	
Time from diagnosis (day)	Mean (SD)	416.3 (380.2)	369.2 (330.7)	0.460
Race (%)				
	Caucasian	58 (98.3%)	60 (98.4%)	1.000
	Black	0 (0.0%)	0 (0.0%)	
	Asian/Pacific islander	0 (0.0%)	0 (0.0%)	
	Other	1 (1.7%)	1 (1.7%)	
Study disease (%)				
	a-MCI	38 (61.3%)	42 (67.7%)	0.453
	vm-AD	24 (38.7%)	20 (32.3%)	
MMSE Baseline (PP)	Mean (SD)	25.7 (1.5)	26.2 (2.1)	0.197
RBANS Baseline (PP)	Mean (SD)	66.3 (9.4)	68.5 (13.1)	0.323
CDR Baseline (PP)	Mean (SD)	0.5 (0.0)	0.5 (0.0)	1.000
ADCS-MCI-ADL Baseline (PP)	Mean (SD)	52.5 (9.8)	53.04 (8.3)	0.774

PP= Per Protocol Population

- Demographics and baseline characteristics were **well balanced** across the groups
- Baseline **cognitive status** defined by MMSE, RBANS, CDR and ADCS-ADL tests **were the same in both groups**

Figure 1: Baseline amyloid–PET status

2. Primary safety endpoint

Table 2: Summary of Treatment Emergent AE

	Safety population (N=124)		
	ABvac40 (n= 62)	Placebo (n= 62)	P-value
Patients with an AE, n (%)	56 (90.3%)	60 (96.8%)	0.144
Patients permanently discontinuing treatment due to AE, n (%)	4 (6.5%)	7 (11.3%)	0.343
Patients with a treatment-caused AE, n (%)	31 (50.0%)	31 (50.0%)	1.000
Patients with a serious AE (SAE)	15 (24.2%)	18 (29.0%)	0.542
Patients with a treatment-caused SAE, n (%)	3 (4.8%)	7 (11.3%)	0.187
Number of all-cause deaths, n (%)	1 (1.6%)	1 (1.6%)	1.000

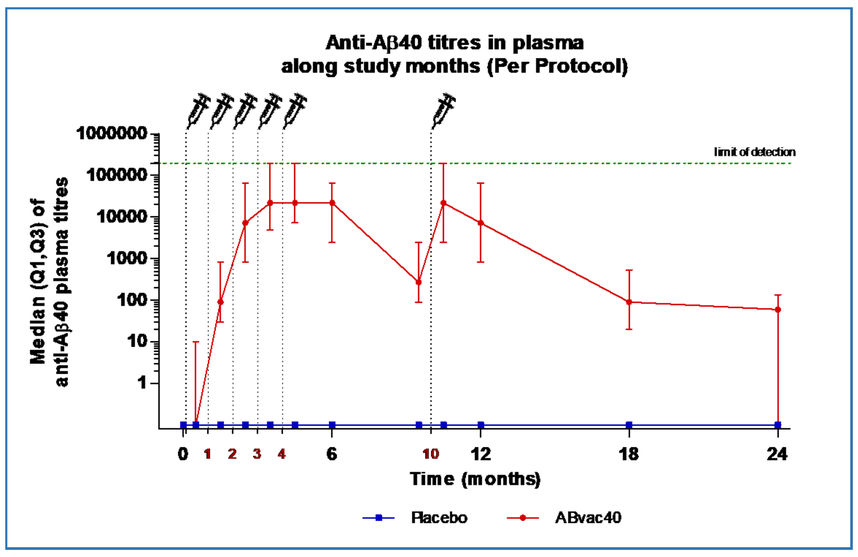
- **No differences observed** in Treatment Emergent Adverse events **between groups**
- **No differences observed in a total of adverse** event (ABvac40= 395 in 56 patients; Placebo= 389 in 60 patients) between groups

Table 3: Adverse events with incidence > 10% and Imaging safety findings

	Safety population (N=124)		
Patients with any event, n (%)	ABvac40 (n= 62)	Placebo (n= 62)	p-value
Injection site reacction and General disorders	31 (50.0%)	30 (48,4%)	0.857
Urinary tract infection (*none were considered related to IMPD*)	13 (21.0%)	6 (9,6%)	0.081
Fall (none were considered related to IMPD)	10 (16.1%)	5 (8.1%)	0.169
ARIA-H	8 (12.9%)	7 (11.3%)	0.783
Cerebellar infarction (considered not related to IMPD)	1 (1.6%)	0 (0.0%)	1.00
Cerebral hemorrhage	0 (0.0%)	1 (1.6%)	1.00
Cerebral infarction	0 (0.0%)	1 (1.6%)	1.00
Lacunar infarction (considered not related to IMPD)	1 (1.6%)	0 (0.0%)	1.00
Superficial siderosis	0 (0.0%)	2 (3.2%)	0.496
Headache	7 (11.3%)	9 (14.5%)	0.667
Erythema	10 (16.1%)	7 (11.3%)	0.604

- **No difference observed in a total ARIA-H events** (ABvac40; 9 vs Placebo; 12) between groups
- **No differences observed in brain hemorrhagic events between groups**

3. Primary Efficacy (Immunogenicity) Endpoint



- **ABvac40 elicited a consistent and specific immune response against the C-terminal end of Aβ40**
- Plasma **anti-Aβ40 titres decrease with time**
- **A booster dose** 6 months after the last injection **increased anti-Aβ40 titres**

CONCLUSIONS

- ✓ **The repeated administration of ABvac40 in patients diagnosed with aMCI and very mild AD demonstrated to be safe and tolerable. Remarkably, incidence of ARIA-H was equal for both groups**
- ✓ **ABvac40 induced a strong immune response characterized by an increase of anti-Aβ40 titres that parallels with an increase of total plasma levels of Aβ40**
- ✓ **Secondary exploratory efficacy endpoints are under analysis**
- ✓ **Part B of the study is progressing as planed**