Araclon Biotech GRIFOLS

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

hallmarks main One Of the OŤ Alzheimer's disease (AD) is the deposition of amyloid- β peptides (A β) in the neuropil and blood vessels. Araclon Biotech is developing ABvac40, an active vaccine against AB40 peptide,

TOP LINE DATA (Part A)

Fable 1: DemographicsAbvac 40 (n= 62)Placebo (n= 62)P-valueageMean (SD)70.6 (6.0)70.1 (5.5)0.629aducation (%)Some school25 (40.3%)16 (25.8%)14 (5.8%)1	. Demographics and baseline characteristics					
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DCS-MCI-ADL Baseline (PP) Mean (SD) 52.5 (9.8) 53.04 (8.3) 0.774 P= Per Protocol Population 52.5 (9.8) 53.04 (8.3) 0.774	DR Baseline (PP)	Mean (SD)	0.5 (0.0)	0.5 (0.0)	1.000	
-	DCS-MCI-ADL Baseline P= Per Protocol Population	e (PP) Mean (SD)	52.5 (9.8)	53.04 (8.3)	0.774	

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		

one of the peptides present in senile plaques and the dominant peptide in vascular deposits, that has been with associated 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 AB is cleaved and secreted. In a Phase 1 clinical trial (NCT03113812), ABvac40 showed to be safe and tolerable and а long-lasting antibody generated response (56 weeks) after only threemonthly immunizations (Lacosta et al, Alzheimer's Research & Therapy 2018).

- Demographics and baseline characteristics were
- 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

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

METHODS

In 2017, Araclon Biotech initiated a multicenter, Phase 2, 24-month, double-blind, placeborandomized, controlled trial in patients with a-MCI or vm-AD investigate the safety, to 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.

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

	Safety population (N=124)			
Table 2: Summary of Treatment Emergent AE	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	



- 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

STUDY DESIGN



- **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

CONCLUSIONS

 \checkmark 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-AB40 titres that parallels with an increase of total plasma levels of Aβ40
- Secondary exploratory efficacy endpoints are under analysis
- \checkmark Part B of the study is progressing as planed