AB1601 phase 2 study of ABvac40, an anti-Aβ40 vaccine: safety and immunogenicity of a cross-over extension

María Pascual-Lucas[1], Ana M Lacosta[1], Jesús Canudas[1], María Montañés[1], José A Allué[1], Leticia Sarasa[1], Elisabet Molina[1], Sergio Castillo[1], Manuel Sarasa[1†], Jose Terencio[1,2], Mercè Boada[3]

(1) Araclon Biotech, Zaragoza, Spain, (2) Grifols, Barcelona, Spain, (3) Ace Alzheimer Center Barcelona, Universitat Internacional de Catalunya, Barcelona, Spain, † Deceased May 27, 2020

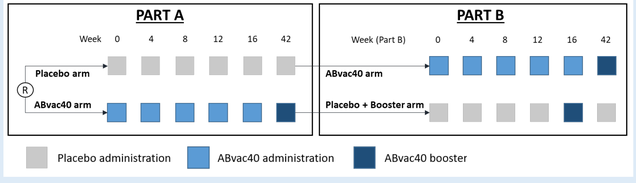
BACKGROUND

Previous studies suggested that Aβ40 could have an important role in Alzheimer's disease (AD), especially in relation to amyloid deposition in blood vessels. AB1601 (NCT03461276) is a multicenter, randomized, double-blind, placebo-controlled, phase 2 study in patients with amnestic mild cognitive impairment (a-MCI) or very mild AD (vm-AD) to investigate safety, tolerability and immunogenicity of repeated subcutaneous injections of ABvac40, a vaccine targeting Aβ40. The 24-month study (Part A) showed that ABvac40 was safe, well-tolerated and highly immunogenic. An additional 18-month cross-over study (Part B) was conducted to evaluate safety and immunogenicity in patients randomized to placebo in Part A, and to assess safety and immunogenicity of a delayed booster of ABvac40 in ABvac40-treated patients in Part A.

METHODS

A total of 124 patients with a-MCI (N=80) or vm-AD (N=44) were initially included in Part A and randomized to ABvac40 (N=62) or Placebo (N=62). Seventy-seven out of 101 patients who completed Part A transitioned to Part B. Safety assessments included the frequency of ARIA and aseptic meningo-encephalo-myelitis as treatment emergent serious adverse events of special interest. Immune response was assessed by quantification of concentration of specific anti-Aβ40 antibodies in plasma and CSF. Aβ40 peptide levels in plasma were measured by ABtest-MS (Araclon Biotech).

STUDY DESIGN



All results reported here are preliminary results

BASELINE CHARACTERISTICS

Characteristic	ABvac40 arm Part A / Placebo + Booster arm Part B (N=62)	Placebo arm Part A / ABvac40 arm Part B (N=62)
Age (years), mean (SD)	70.6 (6.0)	70.1 (5.5)
Female, n (%)	38 (61.3)	36 (58.1)
ApoE ε4 status, n (%)		
Non-carriers	24 (38.7)	24 (38.7)
Carriers: Heterozygous	29 (46.8)	33 (53.2)
Carriers: Homozygous	9 (14.5)	5 (8.1)
Amyloid-PET status, n (%)		
Positive	47 (75.8)	45 (72.6)
Negative	15 (24.2)	17 (27.4)
Study disease, n (%)		
a-MCI	38 (61.3)	42 (67.7)
vm-AD	24 (38.7)	20 (32.3)
MMSE score, mean (SD)	25.7 (1.55)	25.9 (2.1)

ITT analysis set. ApoE: Apolipoprotein E. MMSE: Mini-Mental State Examination

SAFETY

Neither ARIA-E nor aseptic meningo-encephalo-myelitis were reported. **ARIA-H incidence was low and equally distributed** in both treatment groups

Treatment Emergent SAESI	ABvac40 (N=99)		Placebo (N=62)	
	Number of patients (%)	Total number of events	Number of patients (%)	Total number of events
ARIA-E	0 (0.0)	0	0 (0.0)	0
ARIA-H	9 (9.1)	10	7 (11.3)	10
Meningo-encephalo-myelitis	0 (0.0)	0	0 (0.0)	0

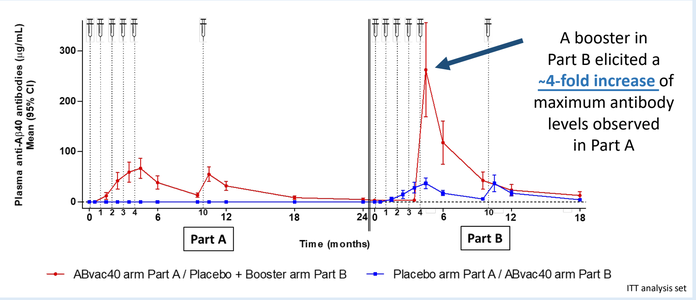
Safety analysis set. SAESI: Serious Adverse Events of Special Interest. ARIA: Amyloid Related Imaging Abnormalities. E: Edema. H: hemorrhage

ABvac40 includes all patients who took at least one dose of ABvac40 in both the ABvac40 arm Part A / Placebo + Booster arm Part B treatment sequence, and ABvac40 arm Part B. **Placebo** includes all patients in the Placebo arm Part A who took at least one dose of Placebo.

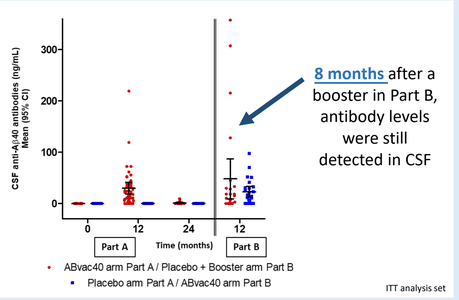
Total number of events refers to the number of ARIAs reported as new SAE events (excluding follow-up SAEs).

IMMUNOGENICITY

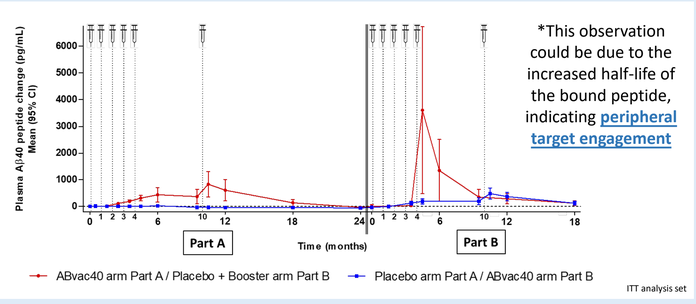
ABvac40 elicited a **high concentration of specific anti-Aβ40 antibodies** in plasma throughout the study



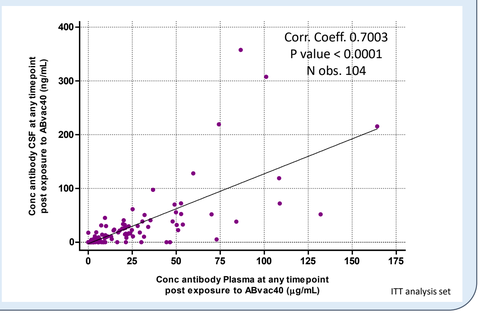
Anti-Aβ40 **antibodies were detected in CSF**, with a CSF:plasma ratio of 0.1%



Plasma levels of Aβ40 paralleled the anti-Aβ40 antibodies increase*



Anti-Aβ40 antibody levels **significantly correlated** between **plasma and CSF**



CONCLUSIONS

- **ABvac40 showed an excellent safety profile related to ARIA-E, ARIA-H and aseptic meningo-encephalo-myelitis** during a follow-up of 36-42 months.
- ABvac40 elicited a **strong, specific and sustained immune response in plasma** with a **4-fold increase** after a **booster** in Part B.
- Antibodies were detected in **CSF, correlating with plasma levels,** with **penetrating rates** comparable to other immunotherapies.
- These findings suggest ABvac40 **potential for combination** with other complementary disease-modifying therapies.
- **Final study results**, including exploratory efficacy endpoints, will be available in **Q4 2023**.