Supplemental Material S1: Key Inclusion and Exclusion for Study 201, 202, and 251

Key inclusion criteria for study 201 were:

- Eligible patients were aged 50 to 85 years, inclusive
- National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS/ADRDA) criteria for probable Alzheimer's disease (AD)
- MRI consistent with AD
- Mini-Mental State Examination (MMSE) score of 16–26
- Rosen-Modified Hachinski Ischemic score ≤ 4

Key exclusion criteria for study 201 were:

- Clinically significant neurologic disease other than AD
- Major psychiatric disorder, or history of stroke or seizures
- Hamilton Rating Scale score for depression ≥ 12
- Current use of anticonvulsant, antiparkinsonian, anticoagulant, or narcotic medications; recent immunosuppressive or cancer chemotherapy medications; or cognitive enhancers other than acetylcholinesterase inhibitors or memantine at a stable dose for at least 120 days before screening

Key inclusion/exclusion criteria for study 202 were similar to 201 except that:

- Patients were aged 50–80 years, inclusive
- Amyloid-β loads were required to be in the range expected for patients with Alzheimer's disease, defined as 11C-PiB PET retention ratios relative to the cerebellum of 1·5 or more in at least three brain regions among the anterior cingulate, posterior cingulate, frontal, temporal, and parietal cortices
- MMSE score of 18–26 was required

Key inclusion/exclusion criteria for study 251 were similar to 201 and 202 except that:

- Patients were required to have completed study 201

- Patients were additionally excluded if they had a screening visit brain MRI scan (ie, study 201 or study 202 week 71 MRI scan) indicative of any other significant abnormality, including but not limited to multiple microhemorrhages or evidence of a single prior hemorrhage >1 cm3; multiple lacunar infarcts or evidence of a single prior infarct >1 cm3; evidence of a cerebral contusion, encephalomalacia, arachnoid cysts; or brain tumors (eg, meningioma) unless approved by the medical monitor

Supplemental Material S2: Proportional Hazards Regression Models (Sensitivity Analysis With Follow-up Time Truncated to 323 Days)

Reduced Models Possible Factor HR (95% CI) (p-value)	Level	Univariate Models HR (95% CI) (p-value)	Full Models HR (95% CI) (p-value)
Dose 5.78 (0.69, 48.25) (0.1051)	0.5 mg/kg vs. 0.15 mg/kg	4.99 (0.60, 41.46) (0.1367)	5.06 (0.60, 42.89) (0.1373)
6.49 (0.84, 50.28) (0.0736)	1.0 mg/kg vs. 0.15 mg/kg	7.33 (0.95, 56.80) (0.0565)	6.38 (0.82, 49.49) (0.0761)
19.67 (2.54, 152.11) (0.0043)	2.0 mg/kg vs. 0.15 mg/kg	16.03 (2.08, 123.34) (0.0077)	18.40 (2.37, 143.03) (0.0054)
ApoE e4 Genotype 5.49 (1.55, 19.45) (0.0084)	Heterozygote vs. No alleles	4.08 (1.18, 14.09) (0.0263)	5.12 (1.44, 18.24) (0.0118)
12.15 (3.40, 43.44) (0.0001)	Homozygote vs. No alleles	10.84 (3.06, 38.45) (0.0002)	12.55 (3.51, 44.90) (0.0001)
White Matter Hyperintensities	Confluent or diffusion lesions vs. None or punctuate	1.90 (0.78, 4.66) (0.1581)	1.89 (0.73, 4.92) (0.1902)
Small Hemosiderin Deposits	Present (one or more) vs. Absent (none)	0.68 (0.16, 2.85) (0.5971)	0.77 (0.18, 3.33) (0.7261)

Patients with missing ApoE e4, white matter hyperintensity at baseline and small hemosiderin deposit at baseline are excluded.
Univariate Models: Each factor is alone in the model.
Full Model: All factors are in the model; thus, each factor may be considered adjusted for the other factors.
Reduced Model: Only the factors with estimates are in the model; specifically, dose and ApoE e4 genotype.
HR = hazard ratio
CI = confidence interval
ApoE e4 = apolipoprotein E epsilon 4 allele frequency

The proportional hazards analyses models presented in Tables 1 and 2 were tested for deviation from the proportional hazards assumption using log, negative log plots; no obvious violations of the proportional hazards assumption were observed even beyond the first year. Nevertheless, due to the fact that relatively few events occurred after the first year, and that these might have been disproportionally influential, we addressed this issue by performing a sensitivity analysis in which all observations were censored at 323 days. This follow-up period was selected as this was the number of days following the first dose up to and including the MRI scheduled after the 3rd infusion. For these analyses as well, the log, negative log plots showed no obvious violations of the proportional hazards assumption. Additionally, the models were evaluated with each factor along with its time interaction term, and all p-values for the interaction terms were above 0.15, again supporting the appropriateness of the PH model. The results of the sensitivity analysis are consistent with the analyses with complete follow-up. Although the magnitudes of the point estimates may differ, they are directionally similar. Time interactions were evaluated for the co-factors, ApoE and small hemosiderin deposits, in the models without truncation and were not found to be statistically significant at the 0.05 level.

Supplemental Material S3: Table of Symptomatic Patients

Patient	Age	Gender	ApoE Genotype	Dose (mg/kg)	Number of infusions prior to ARIA-E occurrence	Hospitalized	MRI Abnormality: Time to Resolution (Days)	Treatment	Clinical symptoms
1	58	F	E4/E4	1.0 mg/kg	1	Y	78	acetaminophen (for headache)	upper abdominal pain (mild), headache (mild), confusional state (mild), hallucination (mild), visual field defect (mild), disorientation (mild), decreased appetite (mild), vomiting (mild), apraxia (mild)
2	71	M	E4/E4	2.0 mg/kg	1	N	119	none	irritability (moderate), forgetfulness (moderate), ataxia (moderate), confusion (moderate), agitation (moderate)
3	66	F	E4/E4	2.0 mg/kg	1	N	182	none	fatigue (mild)
4	64	F	E3/E4	2.0 mg/kg	1	Y	36	dexamethasone	lethargy (severe), confusional state (moderate), gait disturbance (mild), headache (moderate)
5	83	M	E3/E4	2.0 mg/kg	1	N	197	none	headache (mild)

6	84	F	E4/E4	0.15 mg/kg	2	Y	52	hydrochlorothiazide (for elevated blood pressure, ongoing prior to/during trial)	gait disturbance (moderate), cognitive disorder (moderate)
7	78	F	E4/E4	0.5 mg/kg	4	Y	17	dexamethasone	ataxia (severe), aphasia (severe), depressed level of consciousness (severe)
8	72	F	E3/E3	1.0 mg/kg	2	N	143	none	throbbing headache (severe), incoordination (severe)