Evidence Table 1. Individual Phase-3 RCTs of monoclonal antibodies versus placebo in Alzheimer's Disease: Summary-level information

Monoclonal Antibody (Dose)	Years of Trial "Trial Name" NCT#	Author & Year	AD Stage & MMSE Scores of Patients Included	Sample Size (I; C) # of Sites	Mean Years of Age, I; C	Percent Female I; C	Percent by Race/Ethnicity I; C	Mechanism(s) of Action	Aim	Trial Duration (wks)	Primary Efficacy Outcome & Whether Achieved	Statistically Significant Secondary Outcomes (Functional & Cognitive)	ARIA[b] Percent (I; C) Unless NS	Completed[c]
BAPINEUZUMAB														
Bapineuzumab (0.5 mg/kg)[f]	6/2008-10/2012 "Non-carrier Study (3000)" NCT00667810	Vandenberghe: 2016	Mild-Moderate AD; MMSE: 16-26[d] (APOE-ε4 non-carriers)	N=583 (255; 328) 265 sites	71.1; 69.7	55.7; 57.9	White 79.2; 80.5 Black 0.8; 0.6 Asian 17.3; 17.1 Other 2.7; 1.8	Antibodies bind to any Aβ conformation (Monomer, oligomer, fibril)	Clear Aβ	78	ADAS-Cog11, DAD[e] (Not Achieved)	None	ARIA-E: 4.9%; 0.5%	NC-Fut
Bapineuzumab (1.0 mg/kg)[f,g]	6/2008-10/2012 "Non-carrier Study (3000)" NCT00667810	Vandenberghe: 2016	Mild-Moderate AD; MMSE: 16-26 [d] (APOE-ε4 non-carriers)	N=581 (253; 328) 265 sites	70.7; 69.7	57.3; 57.9	White 79.4; 80.5 Black 2.0; 0.6 Asian 17.4; 17.1 Other 1.2; 1.8	Antibodies bind to any Aβ conformation (Monomer, oligomer, fibril)	Clear Aβ	78	ADAS-Cog11, DAD[e] (Not Achieved)	None	ARIA-E: 11.8%; 0.5%	NC-Fut
Bapineuzumab (0.5 mg/kg)[f]	1/2008-10/2012 "Carrier Study (3001)" NCT00676143	Vandenberghe: 2016	Mild-Moderate AD; MMSE: 16-26 [d] (APOE-ε4 carriers)	N=1081 (650; 431) 222 sites	70.9; 70.2	64.5; 60.1	White 79.5; 82.6 Black 0.8; 0.7 Asian 17.7; 16.0 Other 2.0; 0.7	Antibodies bind to any Aβ conformation (Monomer, oligomer, fibril)	Clear Aβ	78	ADAS-Cog11, DAD[e] (Not Achieved)	None	ARIA-E: 16.7%; 2.1%	NC-Fut
Bapineuzumab (0.5 mg/kg)	12/2007-6/2012 "Non-carrier Study (301)" NCT00574132	Salloway: 2014	Mild-Moderate AD; MMSE: 16-26 (APOE-ε4 non-carriers)	(337; 524) 861 N=807 (314; 493) 218 sites	73.0; 71.8 73.1; 71.9	51.9; 50.8	White 93.2; 93.9	Antibodies bind to any Aβ conformation (Monomer, oligomer, fibril)	Clear Aβ	78	ADAS-cog11, DAD[h] (Not Achieved)	None	ARIA-E: 4.2%; 0.2%	C-PON
Bapineuzumab (1.0 mg/kg)[i]	12/2007-6/2012 "Non-carrier Study (301)" NCT00574132	Salloway: 2014	Mild-Moderate; MMSE: 16-26 (APOE-ε4 non-carriers)	(329; 524) N=853 218 sites	73.2; 71.8	56.5; 50.8	White 93.3; 93.9	Antibodies bind to any Aβ conformation (Monomer, oligomer, fibril)	Clear Aβ	78	ADAS-cog11, DAD (Not Achieved)	None	ARIA-E: 9.4%; 0.2%	C-PON
Bapineuzumab (.5 mg/kg)	12/2007-4/2012 "Carrier Study (302)" NCT00575055	Salloway: 2014	Mild-Moderate AD; MMSE: 16-26 (APOE-ε4 carriers)	N=1121 (673; 448) 170 sites	72.1; 72.4	54.8; 56.3	White 94.7;96.2	Antibodies bind to any Aβ conformation (Monomer, oligomer, fibril)	Clear Aβ	78	ADAS-cog11, DAD (Not Achieved)	None	ARIA-E: 15.3%; 0.2%	C-PON
SOLANEZUMAB														
Solanezumab (400 mg IV)[o]	5/2009-4/2012 "EXPEDITION 1 (ORIGINAL)" NCT00905372	Doody: 2014	Mild-Moderate AD; MMSE: 16-26	N=1012 (506; 506) 111 sites	75.0; 74.4	59.1; 56.7	White 83.0; 84.4 Black/African American 4.0; 4.9 Asian 12.8; 9.7 American Indian/Alaska Na 0; 0.4 >1 cat 0.2; 0.6	Antibodies bind to one Aβ conformation (Monomer only)	Clear Aβ	80	ADAS-Cog11, ADCS-ADL[q,s] (Not achieved)	None	NS[w]	C-PON
Solanezumab[o] (400 mg IV)	5/2009-4/2012	Doody: 2014	Mild-Moderate AD;	N=1040	72.5; 72.4	54.3; 55.1	White 76.6; 77.6	Antibodies bind to one Aβ conformation	Clear Aβ	80	ADAS-Cog11,	MMSE	NS[w]	C-PON

	"EXPEDITION 2 (ORIGINAL)" NCT00904683		MMSE: 16-26	(521; 519) 111 sites			Black 1.3; 0.4 Asian 21.5; 22.0 AI/AN 0.2; 0 >1 cat 0.4; 0	(Monomer only)			ADCS-ADL[s] (Not Achieved)			
Solanezumab (400 mg IV)	5/2009-4/2012 "EXPEDITION 2 (Secondary Analysis of *MILD AD ONLY)* [j,t]	Doody: 2014	Mild AD; MMSE: 20-26	~~N=1040~~ (521; 519) 111 sites	72.5; 72.4	54.3; 55.1	White 76.6; 77.6 Black 1.3; 0.4 Asian 21.5; 22.0 Other 0.6; 0.0	Antibodies bind to one Aβ conformation (Monomer only)	Clear Aβ	80	ADAS-Cog14 (Not Achieved); ADCS-ADL (Achieved)	None	NS[w]	C-PON
Solanezumab (400 mg IV)	5/2009-4/2012 "EXPEDITION 2 (Secondary Analysis of *MODERATE AD ONLY*") [j,t]	Doody: 2014	Moderate AD; MMSE: 16-19	N=1040 (521; 519) 111 sites	72.5; 72.4	54.3; 55.1	White 76.6; 77.6 Black 1.3; 0.4 Asian 21.5; 22.0 Other 0.6; 0.0	Antibodies bind to one Aβ conformation (Monomer only)	Clear Aβ	80	ADAS-Cog14, ADCS-ADL[s] (Not Achieved)	MMSE	NS[w]	C-PON
Solanezumab (400 mg IV)	5/2009-4/2012 "EXPEDITIONS 1 & 2 - (Secondary Pooled Analysis of MILD AD ONLY)" [j,t] NCT00905372 & NCT00904683	Doody: 2014	Mild-Moderate AD; MMSE: 16-26	N=2052 (1027; 1025) 111 sites	72.5; 72.4	54.3; 55.1	White 76.6; 77.6 Black 1.3; 0.4 Asian 21.5; 22.0 Other 0.6; 0.0	Antibodies bind to one Aβ conformation (Monomer only)	Clear Aβ	80	ADAS-Cog14, ADCS-ADL[s] (Not Achieved)	None	NS[w]	C-PON
Solanezumab (400 mg IV)	5/2009-4/2012 "EXPEDITIONS 1 & 2" POOLED (Mild only) [j] NCT00905372 & NCT00904683	Siemers: 2016	Mild AD; MMSE: 20-26	N=1012 (659; 663) 111 sites	73.9 73.3	52.5; 54.6	White 80.4; 84.2 Black 2.4; 1.8 Asian 16.8; 13.7 Other 0.3; 0.3	Antibodies bind to one Aβ conformation (Monomer only)	Clear Aβ	80	ADAS-Cog14[v] (Achieved)	ADAS-Cog11 ADAS-Cog14 MMSE ADCS-iADL	NS[x]	C-POY
Solanezumab (400 mg)	7/2013-10/2016 "EXPEDITION 3" NCT01900665	Honig: 2018	Mild AD; MMSE: 20-26	N=2129 (1057; 1072) 210 sites	72.7; 73.3	56.8; 58.9	White 90.5; 90.7 Black 1.4; 1.9 Asian 7.7; 7.2 Other 0.3; 0.2	Antibodies bind to one Aβ conformation (Monomer only)	Clear Aβ	76	ADAS-Cog14 (Not Achieved)	MMSE CDR-SB ADAS-ADL	NS[u]	NC-Fut
GANTENERUMAB														
Gantenerumab (105 mg)	1/2010-9/2020 "Scarlet Road" NCT01224106	Ostrowitzki: 2017	Prodromal AD; MMSE: ≥24	N=537 (271; 266) 128 sites	70.3; 69.5	NR	NR	Antibodies bind to two Aβ conformations (Oligomer & fibril)	Clear Aβ	104	CDR-SB (Not Achieved)	None	ARIA-E: 6.6%; 0.8% ARIA-H(MH): 22.9%; 13.2%	NC-Fut
Gantenerumab (225 mg)	11/2010-9/2020 "Scarlet Road" NCT01224106	Ostrowitzki: 2017	Prodromal AD; MMSE: ≥24	N=526 (260; 266) 128 sites	71.3; 69.5	NR	NR	Antibodies bind to two Aβ conformations (Oligomer & fibril)	Clear Aβ	104	CDR-SB (Not Achieved)	None	ARIA-E: 13.5%; 0.8% ARIA-H(MH): 16.2%; 13.2%	NC-Fut
ADUCANUMAB														
Aducanumab (1-6 mg/kg)	8/2015-8/2019 "EMERGE" (Study 302) NCT02484547	Haeberlein: 2020	Early (MCI & Mild AD); MMSE: 24-30	N=1091 (543; 548) 348 sites	70.6; 70.8	49.5; 52.9	White 79.6%; 78.6% Black 1.1%; 0.2% Asian 7.2%; 8.6% AI/AN 0.0%; 0.2% Other 0.2%; 0.2%	Antibodies bind to one Aβ conformation (Monomer only)	Clear Aβ	78	CDR-SB (Not Achieved)	None	ARIA-E: 25.7%; 2.2% ARIA-H(MH): 16.2%; 6.9% ARIA-H(SS): 9.2%; 2.6%[y,z]	NC-Fut[l]

							NR 12.0%;12.2% Unknown 0.0%; 0.0% Separate measure Hispanic/Latino 4.1%; 4.0%							
Aducanumab (1-10 mg/kg)	8/2015-8/2019 "EMERGE" (Study 302) NCT02484547	Haeberlein: 2020	Early (MCI & Mild AD); MMSE: 24-30	N=1095 (547; 548) 348 sites	70.6; 70.8	51.9; 52.9	White 77.1%; 78.6% Black 0.7%; 0.2% Asian 7.7%; 8.6% AI/AN 0.0%; 0.2% Other 0.5%; 0.2% NR 13.7%;12.2% Unknown 0.2%; 0.0% Separate measure Hispanic/Latino 4.2%; 4.0%	Antibodies bind to one Aβ conformation (Monomer only)	Clear Aβ	78	CDR-SB (Achieved)[l]	ADAS-Cog 13 ADCS-ADL-MCI[i] MMSE CDR-SB SUVR CSF p-tau ADAS-ADL	ARIA-E: 34.0%; 2.2% ARIA-H(MH): 18.6%; 6.9% ARIA-H(SS): 13.3%; 2.6%[y,z]	NC-Fut[l]
Aducanumab (1-6 mg/kg)	8/2015-8/2019 "ENGAGE" (Study 301) NCT02477800	Haeberlein: 2020	Early (MCI & Mild AD); MMSE: 24-30	N=1092 (547; 545) 348 sites	70.4; 69.8	51.9; 52.7	White 75.3%; 75.8% Black 0.2%; 0.9% Asian 10.1%; 10.1% Native Hawaiian or Other Pacific Islander 0.2%; 0%; Other 0.7%; 0.6% NR 13.5%; 12.7% Separate measure Hispanic/Latino 2.0%; 2.4%	Antibodies bind to one Aβ conformation (Monomer only)	Clear Aβ	78	CDR-SB (Not Achieved)	None	ARIA-E: 25.4%; 3.0% ARIA-H(MH): 15.5%; 5.7% ARIA-H(SS): 8.8%; 1.8%[y,z]	NC-Fut[l]
Aducanumab (1-10 mg/kg)	8/2015-8/2019 "ENGAGE" (Study 301) NCT02477800	Haeberlein: 2020	Early (MCI & Mild AD); MMSE: 24-30	N=1100 (555; 545) 348 sites	70.0; 69.8	52.6; 52.7	White 74.4%; 75.8% Black 0.4%; 0.9% Asian 11.7%; 10.1% Native Hawaiian or Other Pacific Islander 0%; 0%; Other 0.5%; 0.6% NR 13.0%;12.7% Separate measure Hispanic/Latino 2.3%; 2.4%	Antibodies bind to one Aβ conformation (Monomer only)	Clear Aβ	78	CDR-SB (Not Achieved)	None	ARIA-E: 35.5%; 3.0% ARIA-H(MH): 17.6%; 5.7% ARIA-H(SS): 15.4%; 1.8%[y,z]	NC-Fut[l]
CRENEZUMAB														
Crenezumab (60 mg/kg)	2020 "CREAD1" NCT02670083	Results on Clinicaltrials.gov	Prodromal to mild AD; MMSE: ≥22	N=813 (404; 409) -	71.0; 70.3	NR	NR	Antibodies bind to any Aβ conformation (Monomer, oligomer, fibril)	Clear Aβ	100	CDR-SB (Not Achieved)	ADAS-Cog	NR	NC-Fut
Crenezumab (100 mg/kg)	2020	Results on Clinicaltrials.gov	Prodromal to mild	N=806	71.1; 70.7	NR	NR	Antibodies bind to any Aβ	Clear Aβ	100	CDR-SB	ADAS-Cog	NR	NC-Fut

	"CREAD2" NCT03114657		AD; MMSE: ≥22	(407; 399) -				conformation (Monomer, oligomer, fibril)			(Not Achieved)	CDR-SB		

a Abbreviations: I: Intervention; C: Control; NR: Not reported or not otherwise found in the literature; ADAS-Cog: Alzheimer's Disease Assessment Scale-Cognitive Subscale; ADCS-ADL: Alzheimer's Disease Cooperative Study-Activities of Daily Living; ADCS-iADL: ADCS instrumental subscale; CANTAB: Cambridge Neuro-psychological Test Automated Battery; CDR-GS: Clinical Dementia Rate-Global Score; CDR-SB: Clinical Dementia Rating-Sum of Boxes; DAD: Disability Assessment for Dementia; DS: Dependence Scale; EQ-5D: European Quality of Life-5 Dimensions; FAQ: Functional Activities Questionnaire. FAQ: Functional Activities Questionnaire; FCSRT: Free and Cued Selective Reminding Test; iADRS: Integrated Alzheimer's Disease Rating Scale; MMSE: Mini Mental State Examination; NPI: Neuropsychiatric Inventory; NTB: Neuropsychological Test Battery; QoL-AD: Quality of Life - Alzheimer's Disease; QOL-AD: Quality of Life in Alzheimer's Disease; RUD-Lite: Resource Utilization in Dementia Lite; SUVR: Amyloid PET standardized uptake value ratio; ZCI-AD Scale Score: Zarit Caregiver Interview for Alzheimer's Disease Scale Score

b ARIA: Amyloid-related Imaging Abnormalities (ARIA); ARIA-E: ARIA with effusion or edema; ARIA-H: ARIA with hemosiderin deposition; ARIA-H(MH): ARIA-H, microhemorrhage; ARIA-H(SS): ARIA-H, superficial siderosis

c C-POY: Completed AND primary outcome was met; C-PON: Completed AND primary outcome was not met NC-AE: Stopped (i.e., not completed) for adverse events; NC-Fut: Stopped (i.e., not completed) for futility;

d "Randomization was stratified by Mini Mental State Examination (MMSE) scores (16–21; 22–26); concomitant cholinesterase inhibitor and/or memantine use; substudy participation; and, in the carrier study, number of copies of ApoE ε4 allele (one allele; two alleles)." (Vandenberghe 2016, p2)

e "Coprimary efficacy endpoints were change from baseline to week 78 in 11-item Alzheimer's Disease Assessment Scale–Cognitive subscale (ADAS-Cog/11) score and Disability Assessment for Dementia (DAD) total score. Change from baseline to week 78 in Dependence Scale, Clinical Dementia Rating–Sum of Boxes (CDR-SOB), and Neuropsychological Test Battery (NTB) total Z-scores were additional endpoints." (Vandenberghe 2016, p2)

f "Patients received a total of six IV infusions of bapineuzumab or placebo every 13 weeks, with brain magnetic resonance imaging (MRI) monitoring for ARIA-E conducted at 6 weeks after each infusion." (Vandenberghe 2016, p,2)

g "Originally, Study 3000 included a bapineuzumab 2.0 mg/kg dose, which was discontinued because of a high rate of clinically symptomatic ARIA-E. Patients randomized to the 2.0 mg/kg group were reassigned to receive 1.0 mg/kg for the remainder of the study, and the randomization ratio was adjusted accordingly." (Vandenberghe 2016, p,2)

h "The coprimary outcome measures, the ADAS-cog11 and DAD scores, were assessed at baseline, at treatment visits, and at week 78. Other cognitive and functional outcome measures included scores on the Neuropsychological Test Battery (which was scored on a standardized z scale, with higher scores indicating less impairment),19 the Clinical Dementia Rating–Sum of Boxes (with scores ranging from 0 to 18 and higher scores indicating greater impairment),20 the MMSE, and the Dependence Scale (with scores ranging from 0 to 15 and higher scores indicating greater need for assistance)." (Salloway 2014, p4)

i "We had initially planned the sample size for the non-carrier study to be approximately 1450 participants, who would be randomly assigned in a 1:1:1:2 ratio to 0.5 mg of bapineuzumab per kilogram, 1.0 mg of bapineuzumab per kilogram, 2.0 mg of bapineuzumab per kilogram, or placebo. However, the sponsor discontinued the 2.0-mg-per-kilogram dose early in the trial on the recommendation of the independent, external data and safety monitoring committee because of a high rate of clinically symptomatic amyloid-related imaging abnormalities with effusion or edema. Participants who had initially been randomly assigned to receive 2.0 mg of bapineuzumab per kilogram (141 participants) were reassigned to the 1.0-mg-per-kilogram group and were included in the safety, but not efficacy, analyses." (Salloway 2014, p4)

j Secondary analysis

k Not included in the NIA meta-analysis

l Aducanumab trials were stopped for futility at interim pooled analysis. The presented analyses are based on secondary analysis of unpooled data. Statistical significance was achieved for high-dose aducanumab with the CDR-SB outcome (p=0.0120)
https://clinicaltrials.gov/ct2/show/results/NCT02484547?term=aducanumab&cond=Alzheimer+Disease&phase=2&draw=2&rank=3

m Increased skin cancer risk

n "On the basis of these findings, and before the EXPEDITION 2 trial was completed, the statistical analysis plan was revised (and resubmitted to regulatory agencies) for analyses of the EXPEDITION 2 data and for analyses of pooled data from EXPEDITION 1 and 2. For these analyses, the patients with mild Alzheimer's disease were considered the primary-analysis population, and the ADAS-cog14, which was designed as a better measure of cognitive change in patients with mild Alzheimer's disease than the ADAS-cog11, was the single primary outcome measure" (Doody 2014, pp. 313-314)

o Statistically significant outcomes and ARIA percent among intervention are presented as pooled between EXPEDITION 1 and 2.

p Increased skin cancer risk

q Efficacy measures included the 11- or 14-item cognitive subscale of the Alzheimer's Disease Assessment Scale (ADAS-cog11 [score range, 0 to 70] and ADAS-cog14 [score range, 0 to 90], with higher scores indicating greater cognitive impairment), the Alzheimer's Disease Cooperative Study–Activities of Daily Living (ADCS-ADL) scale (score range, 0 to 78, with lower scores indicating worse functioning), the Clinical Dementia Rating–Sum of Boxes (CDR-SB), the Neuropsychiatric Inventory (NPI), the Resource Utilization in Dementia Lite (RUD-Lite) scale, the European Quality of Life–5 Dimensions (EQ-5D) scale (proxy version), the Quality of Life in Alzheimer's Disease (QOL-AD) scale, and the MMSE" (Doody 2014, p. 312)

r "After analysis of data from EXPEDITION 1, the primary outcome for EXPEDITION 2 was revised to the change in scores on the 14-item cognitive subscale of the Alzheimer's Disease Assessment Scale (ADAS-cog14; range, 0 to 90, with higher scores indicating greater impairment), in patients with mild Alzheimer's disease."

s "The primary outcomes were the changes from baseline to week 80 in scores on the 11-item cognitive subscale of the Alzheimer's Disease Assessment Scale (ADAS-cog11; range, 0 to 70, with higher scores indicating greater cognitive impairment) and the Alzheimer's Disease Cooperative Study–Activities of Daily Living scale (ADCS-ADL; range, 0 to 78, with lower scores indicating worse functioning)." (Doody 2014, p. 311); "Among patients in EXPEDITION 2 who had mild Alzheimer's disease, there was a significant treatment effect on the change in the ADCS-ADL score, with a modeled difference between groups of 2.3 points (95% CI, 0.2 to 4.4; P=0.04) at week 80." (Doody 2014, p. 317)

t "For these analyses, the patients with mild Alzheimer's disease were considered the primary-analysis population, and the ADAS-cog14, which was designed as a better measure of cognitive change in patients with mild Alzheimer's disease than the ADAS-cog11, was the single primary outcome measure" (Doody 2014, p. 314)

u "There was one case of amyloid-related abnormality of edema or effusions on cerebral imaging in the solanezumab group and two cases in the placebo group." (Honig 2018, p. 326)

v This is a secondary analysis of mild AD participants only from both Expedition studies (1 & 2). "In the pooled mild AD population, less decline from

baseline to endpoint was observed in the solanezumab treatment group versus placebo for the ADAS-Cog14 (primary efficacy outcome measure for the analyses of the pooled data set), as well as some other prespecified cognitive and functional outcomes (ADAS-Cog11, MMSE, and ADCS-iADL; $P < .05$ in all cases). For the ADAS-Cog14 and MMSE, there was a slowing of decline of 34%; for ADCS-iADL, there was a slowing of decline of 18%."

w ARIA results are reported as combined between EXPEDITION 1 and 2: "Amyloid-related imaging abnormalities with edema were observed in 0.9% of patients who received solanezumab and in 0.4% of those who received placebo (P=0.27); amyloid-related imaging abnormalities with hemorrhage were observed in 4.9% and 5.6% of patients, respectively (P=0.49)." (Doody 2014, p.319)

x "There were no differences between the treatment groups in the percentage of subjects with ARIA-E or ARIA-H as determined by MRI (P..05). Thirteen subjects (placebo, four; solanezumab, nine) experienced ARIA-E. Six of the10 for whom the information was available carried at least one apolipoprotein E (APOE)ε4 allele. The time-to-resolution of ARIA-E varied. Of the placebo-assigned sub-jects who had ARIA-E, two showed complete resolution and two showed partial resolution during follow-up. For those assigned solanezumab, five showed complete resolution, three showed partial resolution, and one showed no change in ARIA-E severity during follow-up. There were no clinical symptoms clearly associated with ARIA-E for any subject. One subject reported headache and nausea during the time when ARIA-E was present but this resolved within 24 hours after paracetamol treatment before the ARIA-E resolution. At baseline, 248 subjects 19%) had ARIA-H (placebo, 122; solanezumab, 126). Of these, 132(53%) had only a single ARIA-H. Overall, there was an in-crease in size of preexisting ARIA-H and/or increase in ARIA-H number in 36 subjects in the placebo group(5.6%) and 40 (6.6%) in the solanezumab treatment group(P5.55). There was no difference between treatment groups in the number of categorical increases (P5.32)." (Siemers 2016, p. 117)

y ARIA results are sourced from slide 37 of Biogen presentation: https://investors.biogen.com/static-files/f91e95d9-2fce-46ce-9115-0628cfe96e83.

z "ARIA (-E and/or -H)was observed in 41% of patients treated with a planned dose of 10 mg/kg (454 out of 1105), compared to 10% of patients on placebo. ARIA-E was observed in 35% of patients treated with 10 mg/kg, compared to 3% of patients on placebo. The incidence of ARIA-E was higher in apolipoprotein E ε4 (ApoE ε4) carriers than in ApoE ε4 non-carriers (42% and 20%, respectively). The majority of ARIA-E radiographic events occurred early in treatment (within the first 8 doses), although ARIA can occur at any time. Among patients treated with a planned dose of 10 mg/kg who had ARIA-E, the maximum radiographic severity was mild in 30%, moderate in 58%, and severe in 13% of patients. Resolution occurred in 68% of ARIA-E patients by 12 weeks, 91% by 20 weeks, and 98% overall after detection. 10% of all patients who received 10 mg/kg had more than one episode of ARIA-E. ARIA-H in the setting of ARIA-E associated with the use of 10 mg/kg was observed in 21% of patients treated with 10 mg/kg, compared to 1% of patients on placebo. There was no imbalance in isolated ARIA-H (i.e., ARIA-H in patients who did not also experience ARIA-E) between aducanumab and placebo. There was no imbalance in hemorrhage greater than 1 cm between aducanumab and placebo. Clinical symptoms were present in 24% of patients treated with 10 mg/kg who had an observation of ARIA (-E and/or -H), compared to 5% of patients on placebo. The most common symptom in patients treated with 10 mg/kg with ARIA was headache (13%). Other frequent symptoms were confusion/delirium/altered mental status/disorientation (5%), dizziness/vertigo (4%), visual disturbance (2%), and nausea (2%). Serious symptoms associated with ARIA were reported in 0.3% of patients treated with 10 mg/kg. Clinical symptoms resolved in the majority of patients (88%) during the period of observation. In addition, hypersensitivity reactions of angioedema and urticaria occurred in 1 patient in the placebo-controlled clinical trials." (FDA 2021).