that will test whether an anti-amyloid agent can slow cognitive decline during the preclinical stage of AD.

O1-02-03 DIAN-TU ADAPTIVE PREVENTION TRIAL LAUNCH AND BASELINE DATA

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Table 1
Demographics

	All Amyloid PET participants	Not Elevated Amyloid (Aβ-)	Elevated Amyloid (Aβ+)	
	N = 4487	*N = 3164*	*N = 1323*	P-value[§] Aβ- vs Aβ+
Age – Mean years (S.D.)	71.29 (4.67)	70.95 (4.53)	72.10 (4.89)	<0.0001
Education - Mean years (S.D.)	16.57 (2.86)	16.58 (2.89)	16.54 (2.81)	0.662
Sex				0.689
F	2656 (59%)	1879 (59%)	777 (59%)	
Racial Categories				
American Indian/Alaskan Native	32 (1%)	22 (1%)	10 (1%)	1.000[1]
Asian	171 (4%)	141 (4%)	30 (2%)	0.002[1]
Native Hawaiian/Pacific Islander	2 (0%)	2 (0%)	0 (0%)	1.000[1]
Black/African American	167 (4%)	133 (4%)	34 (3%)	0.029[1]
White	4116 (92%)	2866 (91%)	1250 (94%)	<0.001[1]
Unknown/Not Reported	26 (1%)	18 (1%)	8 (1%)	1.000[1]
Ethnicity				0.192
Hispanic or Latino	142 (3%)	103 (3%)	39 (3%)	
Not Hispanic or Latino	4309 (96%)	3040 (96%)	1269 (96%)	
Unknown	35 (1%)	20 (1%)	15 (1%)	
Marital Status				0.655
Married	3166 (71%)	2223 (70%)	943 (71%)	
Divorced	628 (14%)	438 (14%)	190 (14%)	
Widowed	426 (9%)	304 (10%)	122 (9%)	
Never married	183 (4%)	135 (4%)	48 (4%)	
Unknown	83 (2%)	63 (2%)	20 (2%)	
Participant Retired	3402 (76%)	2397 (76%)	1005 (76%)	0.927
Family History of Dementia	3112 (69%)	2136 (68%)	976 (74%)	0.001
APOE Genotype				
ε2/ε2	25 (1%)	23 (1%)	2 (0%)	0.030[1]
ε2/ε3	448 (10%)	379 (12%)	69 (5%)	<0.001[1]
ε2/ε4	116 (3%)	74 (2%)	42 (3%)	0.121[1]
ε3/ε3	2411 (54%)	1930 (61%)	481 (36%)	<0.001[1]
ε3/ε4	1292 (29%)	683 (22%)	609 (46%)	<0.001[1]
ε4/ε4	139 (3%)	34 (1%)	105 (8%)	<0.001[1]
PET SUVr Mean (S.D.)	1.09 (0.19)	0.99 (0.07)	1.33 (0.18)	<0.0001

[§] Fisher's Exact test for categorical variables and Two-sample t-test with unequal variances were used for continuous variables.
[1] Comparisons across individual Racial Categories and APOE Genotype sub-groups were done using a Fisher's Exact test with a Holm's adjustment to the p-value to account for multiple comparisons.

Table 2
Cognitive Tests and Subjective Report of Functional Decline

	All Amyloid PET participants	Not Elevated Amyloid (Aβ-)	Elevated Amyloid (Aβ+)	P-value Aβ- vs. Aβ+
	N = 4487	*N = 3164*	*N = 1323*	(Covariate Adj*)
PACC - Sum of z-scores Mean (Standard Deviation)	0.00 (2.54)	0.18 (2.45)	-0.43 (2.68)	<0.0001 (<0.0001)
MMSE	28.81 (1.21)	28.84 (1.18)	28.73 (1.28)	0.0115 (0.0789)
FCSRT Free	28.96 (5.59)	29.28 (5.49)	28.21 (5.75)	<0.0001 (<0.0001)
FCSRT Total	47.37 (0.91)	47.41 (0.88)	47.28 (0.99)	<0.0001 (0.0005)
Logical Memory Delay	11.70 (3.21)	11.82 (3.17)	11.42 (3.31)	0.0002 (0.0028)
Digit Symbol	43.77 (8.96)	44.29 (8.93)	42.53 (8.92)	<0.0001 (<0.0001)
CFI-Self	2.03 (2.08)	1.89 (2.01)	2.36 (2.20)	<0.0001 (<0.0001)
CFI-Study Partner	1.26 (1.85)	1.17 (1.77)	1.49 (2.02)	<0.0001 (<0.0001)

* Analysis of Covariance on screening scores, adjusted for screening age, gender and years of education.

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Background: Alzheimer's disease (AD) prevention trials target an earlier stage of the disease based on the idea that earlier intervention before neuron loss and symptom onset will provide improved outcomes. The Dominantly Inherited Alzheimer Network Trials Unit (DIAN-TU) launched the first AD prevention trial in 2012 in a rare population of dominantly inherited AD mutation carriers who are destined to get the disease with near 100% penetrance. Recruitment was completed in 2015 into two parallel drug arms in the DIAN-TU adaptive prevention trial (DIAN-TU APT) platform. A major goal of public-private prevention trials is to make data available to the research community and this presentation will provide comprehensive results of baseline data. **Methods:** The metrics of establishing the DIAN-TU platform, start-up of sites, launch of the trial, screening, enrollment and close of enrollment measures were analyzed. Baseline demographic, clinical, cognitive, genetic, imaging including MRI, amyloid PIB PET, amyloid AV45 PET, tau AV1451 PET and biomarker results were analyzed according to protocol. Measures were compared to prior findings in the DIAN observational study. A process for DIAN-TU data requests was developed, approved, and activated in 2017. **Results:** The DIAN-TU APT platform was established in the first year with protocol, site, operational, and multiple partner start-up in this global trial. As sites were activated, enrollment rate increased with rapid enrollment by the end of the study. 194 participants enrolled to successfully meet enrollment goals within projected timelines. Screen fail rate (19%), recruitment source (47% DIAN-obs, 38% DIAN Expanded Registry), and completion rates of all baseline assessments (99-100%) were excellent. This trial provides comprehensive clinical, cognitive, imaging and biomarker data and samples that are being used in the final analyses and are available to address important scientific and medical questions. **Conclusions:** Clinical prevention trials in AD with multiple AD biomarkers are feasible and can be highly successful, even in a rare population. The results from comprehensive evaluations during trials can provide unique insights into the effects of interventions and promise to accelerate highly effective treatments and preventions for AD.

O1-02-04 BASELINE CHARACTERICS FROM A PHASE 3 TRIAL OF CRENEZUMAB IN PRODROMAL TO MILD ALZHEIMER'S DISEASE (CREAD)

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Background: Crenezumab is a humanized anti-amyloid-beta (Aβ) monoclonal IgG4 antibody in development for Alzheimer's disease (AD). Crenezumab binds to multiple forms of Aβ, with high affinity for oligomers, blocking oligomer-induced neurotoxicity, and with low risk of amyloid-related imaging abnormalities (ARIA). Although Phase 2 co-primary endpoints were not met, exploratory analyses suggested that crenezumab should be tested for clinically meaningful efficacy at a higher dose and earlier disease stage. Data from a Phase 1b study that investigated the safety/tolerability of higher doses of crenezumab supported a 4-fold higher Phase 3 dose than used in Phase 2. Two global, randomized, double-blind, placebo-controlled, parallel-group Phase 3 studies (CREAD [NCT02670083]; CREAD2 [NCT03114657]) are testing the efficacy and safety of crenezumab (60 mg/kg) in patients with prodromal to mild AD. Here we describe the study design/methodology, and baseline characteristics from CREAD. **Methods:** Patients aged 50–85 years with prodromal to mild AD and confirmed evidence of cerebral amyloid pathology (CSF or amyloid PET) were enrolled. At screening, patients had an MMSE score of $\geq$22, a CDR-global score of 0.5 or 1, Free and Cued Selective Reminding Test (FCSRT) immediate free recall $\leq$27 and cueing index $\leq$0.67 (to enrich for patients with greater likelihood of progression over 105 weeks), and were randomized 1:1 to placebo or crenezumab (60 mg/kg q4w IV). Randomization was stratified by dementia and APOE status, baseline anti-dementia medications, and geographic region. Primary and secondary endpoints include change from baseline in CDR-SB, ADAS-Cog-13, and ADCS-ADL scores over 105 weeks. Exploratory objectives are to assess treatment effects on CSF biomarkers and amyloid- and tau-PET. MRI examinations are used to monitor safety and measure volumetric changes. **Results:** The CREAD study has completed recruitment, with 813 patients enrolled. Baseline data will be presented. **Conclusions:** Building on learnings from Phase 2, the CREAD and CREAD2 Phase 3 trials are investigating the clinical efficacy of a 4-fold higher dose of crenezumab (vs. Phase 2) in prodromal to mild AD, and will test whether clinically meaningful efficacy can be achieved without the associated safety findings that have been described with other passive anti-amyloid immunotherapies targeting fibrillar amyloid in AD.

O1-02-05 PREDICTING AMYLOID BURDEN IN SCREENING FOR PRECLINICAL AD PREVENTION TRIALS

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Background: Current secondary prevention trials are recruiting participants with evidence of elevated amyloid burden using amyloid PET imaging. Here we explore the best combination of predictors of florbetapir PET SUVR using screening data from the Anti-Amyloid Treatment in Asymptomatic AD (A4) Study. The resulting prediction algorithm could be useful as a prescreen to reduce the number of PET scans required in a future secondary prevention trial. **Methods:** We apply random forest machine learning methods using demographic variables and measures of cognition and function. We consider models with and without APOE genotype. We evaluate the estimated out-of-sample predictive accuracy of each random forest in predicting amyloid burden in independent validation sets while maintaining a detection prevalence of 50% (proportion predicted to be Aβ+). **Results:** Figure 1 shows ROC curves for