Alzheimer’s Prevention Initiative
Treatment Trials

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1. Preclinical AD treatment/biomarker development trials in people who, based on their age & genetic background, are at the highest imminent risk of AD symptoms, beginning with:
   • Autosomal dominant AD mutation carriers close to their estimated age at clinical onset
   • \textit{APOE} ε4 homozygotes close to their estimated age at clinical onset
2. Prevention registries to support these & other trials
   • \textasciitilde 3,400 \textit{E280A PSEN1} mutation kindred members in Antioquia, Colombia enrolled in API Colombia Registry
   • \textasciitilde 28,000 people enrolled in web-based Alzheimer’s Prevention Registry (www.endALZnow.org)
API Trials: Aims

1. Evaluate anti-amyloid therapies in the preclinical treatment of autosomal dominant AD and in people who are APOE ε4 homozygotes
2. Provide better tests of the amyloid hypothesis
3. Help qualify biomarkers for use as reasonably likely surrogate endpoints in preclinical AD trials
4. Provide a foundation for other preclinical AD trials
5. Complement, support & benefit from other initiatives (including the DIAN & A4 trials)
6. Provide a resource of data & samples to the scientific community after the trial is over
7. Offer persons at highest imminent risk for symptoms of AD access to investigational treatments
8. ...and more trials to come
Antioquia, Colombia: A genetically isolated area with strong founder effect for an autosomal dominant mutation causing early onset AD
Double-blind, placebo-controlled trial for up to 60 months with crenezumab 300 mg SC q 2 weeks.

Primary endpoint: change in the API composite cognitive score.

24-month interim analysis using several cognitive/clinical endpoints, & florbetapir PET, FDG PET, MRI, CSF.

Enrollment began in 2013; Clinicaltrials.gov Identifier: NCT01998841
Double-blind, placebo-controlled trial for up to 60 months; treatment TBD

Primary endpoint: change in the API composite cognitive score
24-month interim analysis using cognitive/clinical endpoints, & amyloid PET, FDG PET, MRI, CSF; tau PET

Participants are disclosed their APOE4 genetic status. API exploring potential cohort study of people who learned genetic status (homozygotes and non-homozygotes) and not enrolled in the trial.

Anticipated start date: 2015
Unique Challenge: Recruitment
API Colombia Registry

E280A Population
25 families
5000 members

People Registered
3407

Non Carriers
2543

Carriers
852

Not Genotyped
12

25.01% of those genotyped are carriers

Alive
823

Death
29
Alzheimer’s Prevention Registry Overview

• Launched in May 2012 to accelerate enrollment into coming prevention studies
• Intended to be a shared resource to the scientific community
• Enrollees provide minimal information at sign-up, receive emails notifying individuals about study opportunities within their communities
• Complements other national efforts (TrialMatch) and local registry efforts
• Modeled after other online disease research recruitment registries (Army of Women, Fox Trial Finder)
• Numerous partnerships with academic, government, patient/family advocacy, and corporations
Executive Committee

Jessica Langbaum · Marilyn Albert · Meryl Comer · Jeff Cummings
Jennifer Manly · Ron Petersen · Reisa Sperling · Gabrielle Strobel · Michael Weiner
Pierre Tariot · Eric Reiman · Maria Carrillo (ex officio)
Alzheimer’s Prevention Registry

Who
• Anyone age 18+

Where
• Anywhere in the world, though initial outreach focused on the United States

What & How
• Provide email address, other demographic & contact information at sign up
• Receive email with study opportunities
1,024 US Adults, ages 18-75
Population Representative Distribution
Conducted June 29-July 11, 2012
Margin of error +/- 3.1 percentage points

- Grand-children of Alzheimer’s Sufferers (n=252)
- Adult Children of Alzheimer’s Sufferers (n=218)
- Donors to Disease-related causes (n=212)
- Ages 50+ with Family History of Alzheimer’s (n=274)
Perception of the Registry

Interest In Learning More and Likelihood to Sign Up
(Base: National Adults)

- Interest in Learning More: 73% (Very), 21% (Somewhat)
- Likelihood to Sign Up: 60% (Very), 18% (Somewhat)
- Encourage Others to Sign Up: 63% (Very), 17% (Somewhat)
As an American, it is my duty to help others who are or will be afflicted by Alzheimer’s and the Alzheimer’s Prevention Registry allows me to do this.

My family has a history of Alzheimer’s disease and participating in the Alzheimer’s Prevention Registry is my way to ensure that future generations do not have to deal with this terrible disease.

Medical research on Alzheimer’s disease treatments is very costly, and my participation in clinical trials could help cut costs.

Care for people with Alzheimer’s disease is a costly burden on the national healthcare system, and my participation could help lessen the growing costs of Alzheimer’s care.

Alzheimer’s disease is a major public health crisis. By joining the Alzheimer’s Prevention Registry, I would be helping to protect others against Alzheimer’s.

Widespread participation in clinical trials is key to medical breakthroughs in Alzheimer’s disease. My participation could help prevent me from developing Alzheimer’s disease.

Joining the Alzheimer’s Prevention Registry may benefit or prevent my family or loved ones from suffering from this terrible disease.

% Very/Somewhat Convincing Reason to Join Registry

- Prevent loved ones from suffering: 77%
- Prevent me from developing Alzheimer’s: 73%
- Clinical trials are key to medical breakthroughs: 72%
- Alzheimer’s is a major public health crisis: 71%
- Lessen the growing costs of Alzheimer’s care: 65%
- Could help cut medical research costs: 62%
- My family has a history of AD: 57%
- As an American, it is my duty to help others: 49%
Barriers To Joining the Registry (Top Tier)

% Statement Describes My Point of View About Registry

- Don’t know enough about who is running the registry/how my data would be used: 72%
- Don’t want to be part of a trial to test an unknown drug: 66%
- Concerned about confidentiality of my health data and how it could affect my insurance: 63%
- More concerned about other health issues: 52%

Concerned about confidentiality of my health data and how it could affect my insurance.

At this stage in my life, I am more concerned about other health issues, not Alzheimer’s disease.

I am concerned about the confidentiality of my personal health information if I participate in research and how it could affect my ability to be insured or the cost of my insurance.

I would not want to be part of a trial to test an unknown drug.

Don’t know enough about who is running the Alzheimer’s Prevention Registry and how my data would be used.
Media Coverage Increases Registry Enrollment

The New York Times

AARP Blog

The New Old Age

ADEAR

The Sacramento Bee

The Indianapolis Star

The Huffington Post

The Arizona Republic

Detroit Free Press

USA Today

Oprah.com

FOX News

everyday health.com

because hope matters radio

A place for mom

The Record
Challenges to Increasing Enrollment Numbers (in no particular order!)

• Low awareness about Alzheimer’s prevention research
• Uncertainty about participating in research, what it entails
• No reason to join if not able to join a trial TODAY
• Requires email / Internet access
• Needs of minority groups may differ
• Talks, community events result in few signups
• No survivors to tell their story, motivate others (opposite of breast cancer)
Unique Challenge: Genetic Disclosure
Considerations related to the selection of APOE ε4 HMs for the API Trial

- APOE ε4 HMs are at the highest known risk for LOAD, but their prevalence is ~2-3%
- We have extensive longitudinal data to help inform the design and power of this trial
- REVEAL suggests disclosure of ApoE4 status is well-tolerated
- How to design a clinical trial that enrolls persons at heightened but not certain genetic risk of AD dementia so that the trial:
  - Minimizes risks to subjects
  - Is valid
  - Is feasible in terms of number of subjects and the resources that are required
Engage Potential Participant via trial website

Education, Pre-screen, Electronic Informed Consent

Genetic Testing*

HM(-) Subset - Telephone Prescreen

HM(+) - Telephone Prescreen

Psych Prescreen → F2F Disclosure/Consent for Cohort Study

Psych Prescreen → F2F Disclosure/Consent for Trial

Stop (except for subset)

Stop

Stop

Stop

REMOTE CONTACT

FACE-2-FACE CONTACT

1

2

3

4

5

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Arizona Alzheimer’s Consortium

our colleagues, collaborators, advisors, supporters & research participants
Questions?

BECAUSE YOURS IS A LIFE WORTH REMEMBERING.

endALZnow.org