

MIND Matters

FALL 2022

SPECIAL FEATURE

A Promising Step Forward in Alzheimer's Treatment Development

On September 27th 2022, Eisai and Biogen announced that the topline results of their Phase 3 trial, known as CLARITY, were positive.

This is potentially extremely good news in the effort to develop new therapies for Alzheimer's disease. CLARITY was a placebo-controlled double-blind study of a drug called lecanemab, a monoclonal antibody against the amyloid beta protein, in patients with Mild Cognitive Impairment or mild dementia due to Alzheimer's disease.

Lecanemab has been previously shown to reduce amyloid burden in the brain of patients with symptomatic Alzheimer's disease. According to the initial press release, lecanemab was effective in slowing disease progression measured with the Clinical Dementia Rating Scale (CDR), compared to placebo. These new data could position the drug to be fully approved by the FDA. While some judgment must be reserved until the data are presented and then published, the announcement is exciting. According to the press release, the benefit was observed not only on the primary outcome, but also on key secondary clinical outcomes, including specific measures of cognition (thinking) and function (ability to complete activities of daily living).

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Dear Friends of UCI MIND,

As the fall *MIND Matters* newsletter goes to print, many of us are preparing to travel to San Francisco for the annual Clinical Trials in Alzheimer's Disease (CTAD) meeting, where we will hear important results from recently completed Phase 3 clinical trials of potential new therapies for Alzheimer's disease (AD). This includes trials of lecanemab (page 1) as well as other treatments. The topline results for lecanemab announced by the trial sponsors are exciting and suggest that lecanemab may slow the progression of AD. The availability of treatments to slow the disease would be an exciting and potentially transformative change to patient care.

Yet, disease-slowness is not the same as disease-stopping. Patients living with AD and their families will still face challenges and burden, such as the need to protect the safety of a loved one experiencing cognitive losses by taking away the car keys (page 4). Topics like driving and caregiving, along with the efforts to propel the field forward were covered in our 2022 Southern California AD Research Conference

held in partnership with Alzheimer's Orange County and the Alzheimer's Association, which thankfully returned to in-person this year (page 3). Research will remain essential to further advance the mission to address AD and other dementias. UCI MIND remains committed to this mission and to training the next generation to carry it forward (page 7). This mission is supported by incredible philanthropists like Bob and Virginia Naeve (page 5), Joan and Don Beall (page 7), and many others for whom we are grateful (page 5 and 6).

As 2022 comes to a close, we will take stock of our progress and plot a course forward to have the largest impact and do the greatest good possible. We hope you will do the same and wish you and yours a happy holiday season.



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33rd Annual Research Conference Goes Hybrid

On Friday, September 9th, 2022, UCI MIND, Alzheimer's Orange County, and the Alzheimer's Association Orange County Chapter hosted the 33rd Annual Southern California Alzheimer's Disease Research Conference at the Irvine Marriott.

This year's conference titled, "Dementia Across the Lifespan", was the first one held in person in 3 years and was simultaneously livestreamed to a virtual audience. The theme of the conference addressed different forms of dementia, contextualized by their typical age of onset.

As always, the line-up of speakers was outstanding. The day kicked off with a presentation from esteemed UC Irvine Professor of Pathology and UCI MIND faculty member, Elizabeth Head, PhD, who shared the importance of studying Alzheimer's disease in people with Down syndrome. Jessica Langbaum, PhD, Co-Director of the Alzheimer's Prevention Initiative at Banner Alzheimer's Institute, presented results from a groundbreaking clinical trial in people at risk for a rare genetic form of Alzheimer's disease. Katherine Possin, PhD, Associate Professor of Neurology at UCSF, and Lee Jennings, MD, Associate Professor of Medicine from the University of Oklahoma, presented data from two novel dementia care programs developed at UCSF and UCLA, respectively. Peter Ljubenkov, MD, an Assistant Professor of Neurology from UCSF, spoke on a set of dementias collectively called frontotemporal lobar degeneration.

After a break for lunch, Ahmad Sajjadi, MD, PhD, UCI MIND faculty member and Associate Professor of Neurology and Pathology at UC Irvine, spoke on a newly described form of dementia with an older age of onset called limbic-predominant age related TDP-43 encephalopathy (LATE), and Prashanthi Vemuri, PhD, Professor of Radiology from the Mayo Clinic, discussed how lifestyle factors may influence the unique constructs of resistance and resilience.

The day culminated with a compelling Caregiver Panel, featuring family member representatives for the differing conditions discussed through the day.



Joshua Grill, PhD (left), listens as Ahmad Sajjadi, MD, PhD (right), answers questions from the audience.



Lee Jennings, MD (left) and Katherine Possin, PhD (right) participate in a Q&A session



The Caregiver Panel, including speakers Rosemary Navarro (left), Karen Loeb (left-middle), Kathy Oberst (right-middle), and Dee Ransom (right) answer questions from the audience about their experience caring for loved-ones with dementia.

Navigating Driving and Dementia

Contributed by
Maria Corona, PhD

Dementia broadly refers to a condition that involves cognitive impairment severe enough to interfere with daily life. There are many disorders that can cause dementia, with Alzheimer's disease being the most common.

Individuals with a diagnosis of dementia are at high-risk of having an automobile accident. Driving is a complex activity involving multiple sources of information (e.g., remembering rules of the road, understanding traffic signs) while focusing on the road, manipulating the vehicle, and reacting quickly to a variety of circumstances. Declines in concentration, speed of thinking, decision-making, mental flexibility, and visual-spatial perception that occur in dementia can significantly affect one's driving ability. In many instances, dementia is progressive and thinking abilities will continue to decline to the point at which driving is no longer safe. Some warning signs to look for include feeling less confident while driving, difficulties turning while backing up, being easily distracted, scrapes or dents in the car, poor judgment, slowed reaction times, or getting lost in familiar places.

Laws on driving with dementia vary by state. The California's Health & Safety Code requires physicians to submit a confidential report to the county health department, which is then forwarded to the Department of Motor Vehicles (DMV).

The DMV considers the specific recommendations included in the confidential report, which could be sufficient to elicit the revocation of driving privileges. If the initial report does not elicit an immediate revocation, the DMV will send a notification letter to complete an enclosed Driver Medical Evaluation form. The individual must present this form to their primary physician, authorizing them to submit medical information to the DMV. Upon submission, a Driver Safety officer will review the documentation. Generally, individuals with mild dementia are called



for a re-examination which includes the following steps: (1) vision test, (2) written evaluation, (3) interview, and (4) driving test. If the individual passes, they may be allowed to keep their driving privileges in full or with some restrictions (e.g., no night driving, driving only within a certain radius, or no freeway driving), and this process may be repeated periodically. Alternatively, if the Driver Medical Evaluation form indicates a moderate/severe dementia, driving privileges will likely be revoked. A failure to submit the medical documentation within the requested time frame results in all driving privileges being suspended. In UCI MIND's ADRC research program, our physicians are required to comply with California's mandated reporting laws.

Individuals with dementia may react differently to the loss of their driving privileges. Some may feel relieved, while others may find this transition difficult and may not wish to give up driving. The latter may be particularly true for those who lack insight into their cognitive difficulties. In such cases, it is important for families and providers to collaborate to develop a plan to ensure the individual's safety. One way to approach the conversation is to show understanding and empathy, offer alternatives, and appeal to the individual's sense of responsibility toward the safety of self and others. It may also help to have a document written by a physician with the instructions to not drive to show the individual. As a last resort, it may be necessary to take away the car keys, disable the car, or get rid of it. In any case, it is important that individuals who are no longer permitted to drive continue to have access to safe and reliable alternative transportation.

Wine for the MIND

Everyone was in a festive mood at the annual Wine for the MIND event held on a recent sunny October Sunday afternoon. Virginia and Robert Naeve opened their beautiful home and gardens to collect more than 60 donated wines that will be featured at the *A December to Remember* Gala auction and Wine Pull.

The Naeves served an array of delicious appetizers and wine as guests mingled with UCI MIND faculty researchers, Drs. Joshua Grill, Leslie Thompson, David Sultzer, and Mark Mapstone. These investigators discussed their own research and answered questions from more than 60 guests.

Thank you to the Naeves, who have hosted this event since 2014. It has become a cherished UCI MIND tradition.



Top row: Megan Witbracht, PhD, Anne Quilter / Roger Lisabeth, Bob and Virginia Naeve, Joshua Grill, PhD / Middle row: Wine for the MIND attendees / Cherry Justice, Harriet Harris, Andrea Wasserman / Bottom row: Bob and Virginia Naeve with Dr. Grill / Donated wine

Thank you to our donors



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Year End Gift to Fund Research

As this year draws to a close, our thoughts at UCI MIND turn to you, our friends, donors, research participants, and partners. It is because of your collective effort that we celebrate the many incredible advances we have made in research this year.

- **Thank you** to our research participants, many of whom gathered in August to hear how their contributions to studies have helped advance our research mission.
- **Thank you** to our volunteers who are helping expand outreach to people in Orange County and beyond, especially to underrepresented communities.
- **Thank you** to those volunteers who are willing to educate and advocate for UCI MIND in podcasts, video clips or news articles, or by hosting colleagues and friends at special gatherings with UCI MIND researchers.
- **Thank you** to our philanthropic donors who have made a gift in memory or honor of a friend or loved one.

- **Thank you** to those who sponsor, underwrite, and attend our events including *A December to Remember* Gala or our annual SoCal Alzheimer's Research Conference.
- **Thank you** to each of you who contribute in whatever way you can. Your contribution, small or large, opens the door to innovation and allows UCI MIND to research ways to make memories last a lifetime.
- **Thank you** to those considering making a year-end gift to support UCI MIND in a way that is meaningful to you.

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mind.uci.edu/donate

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Or mail to:
UCI MIND
2646 Biological Sciences III
Irvine, CA 92697-4545

*continued from page 1: A Promising Step Forward
in Alzheimer's Treatment Development*

Overall, the drug also appears to have an acceptable safety profile, with a small proportion (~3%) of participants experiencing symptoms caused by amyloid-related imaging abnormalities in the brain (more patients experienced this side effect without noticeable symptoms). It will be important to learn more about these and other data, including how often people needed to stop taking the drug, how potential unblinding due to side effects was handled, and how many people completed the trial. We are also keenly anticipating learning what effects, if any, were observed on downstream biomarkers such as measures of brain neurofibrillary tangles. Lecanemab is also currently being tested for its potential benefits among those without symptoms due to



To learn more about the AHEAD study,
visit mind.uci.edu/participate

Alzheimer's disease in the AHEAD Study. This study is open to enrollment at UCI MIND and examines whether lecanemab can delay or prevent the onset of symptoms in people age 55-80 who are cognitively unimpaired but who may be at increased risk for Alzheimer's dementia (determined with an amyloid PET scan). Studies like AHEAD are built on the idea that treatments targeting the biology of disease will have the greatest likelihood of success when started as early as possible and aim to reinvent the clinical practice of Alzheimer's disease—moving it toward a chronic, non-fatal condition that can be managed over time to prevent the most disabling stages of disease from occurring.

Beall Scholar Program Comes to Campus



Two Beall Scholars examine a neuropathology specimen. / Ashley Keiser, PhD delivers a talk to the Beall Scholars on animal research. / A Beall Scholar examining a human brain.

With the generous support of Joan and Don Beall, UCI MIND and its trainee organization REMIND hosted the second annual and first-ever in-person Beall Scholar Program from July 18th through the 22nd on the UCI campus.

The goal of the program is to inspire students who are typically underrepresented in STEM fields to pursue careers in brain research and geriatric medicine.



The 2022 Beall Scholar Program class with Drs. Joshua Grill (first row, far left) and Megan Witbracht (first row, second from right) and graduate students and REMIND co-chairs, Michael Neel (first row, far right) and Thuy Lu (second row, far right).

Sixteen rising 12th graders were chosen from a very competitive pool of applicants from Santa Ana and Anaheim Unified School Districts. Half of the chosen scholars will be the first in their family to attend college.

The program included lectures from UCI MIND faculty and trainees on various aspects of neuroscience research and healthcare. The students also experienced lab tours, hands-on demonstrations, and participated in panel discussions on topics including STEM majors, careers in healthcare, and undergraduate opportunities at UCI.



Postdoctoral fellow and REMIND co-chair, Vaisakh Puthusseryppady, PhD, fits a Beall scholar with a virtual reality headset to teach her about his work in spatial navigation and memory. / REMIND co-chair and Neurobiology and Behavior graduate student, Gema Olivarria, mentors two Beall Scholars.

The program provided transportation, meals, and a stipend for all of the scholars who participated. In addition to the week-long curriculum, students were also matched with a graduate student mentor from UCI, who will work with them for the next year to prepare for college.



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