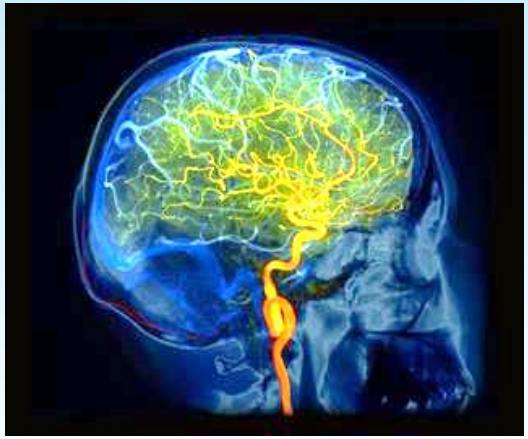
EXHIBIT I

Alzheimer's Disease Drugs Update, 2023

Jeanne Y. Wei, M.D, Ph.D.

Donald W. Reynolds Institute on Aging
and Department of Geriatrics
University of Arkansas for Medical Sciences



Normal Cognitive Aging

- More easily distracted
- Difficulty with multi-tasking
- More time needed to process information
- Diminished working memory
- Diminished visuospatial abilities
- Verbal abilities increase

Early Signs of Dementia

- More repetition
- Difficulty with daily tasks
- Communication difficulties
- Getting lost
- Personality changes
- Confusion about time & place
- Troubling behavior

Wei et al., 2022

Types of Dementia

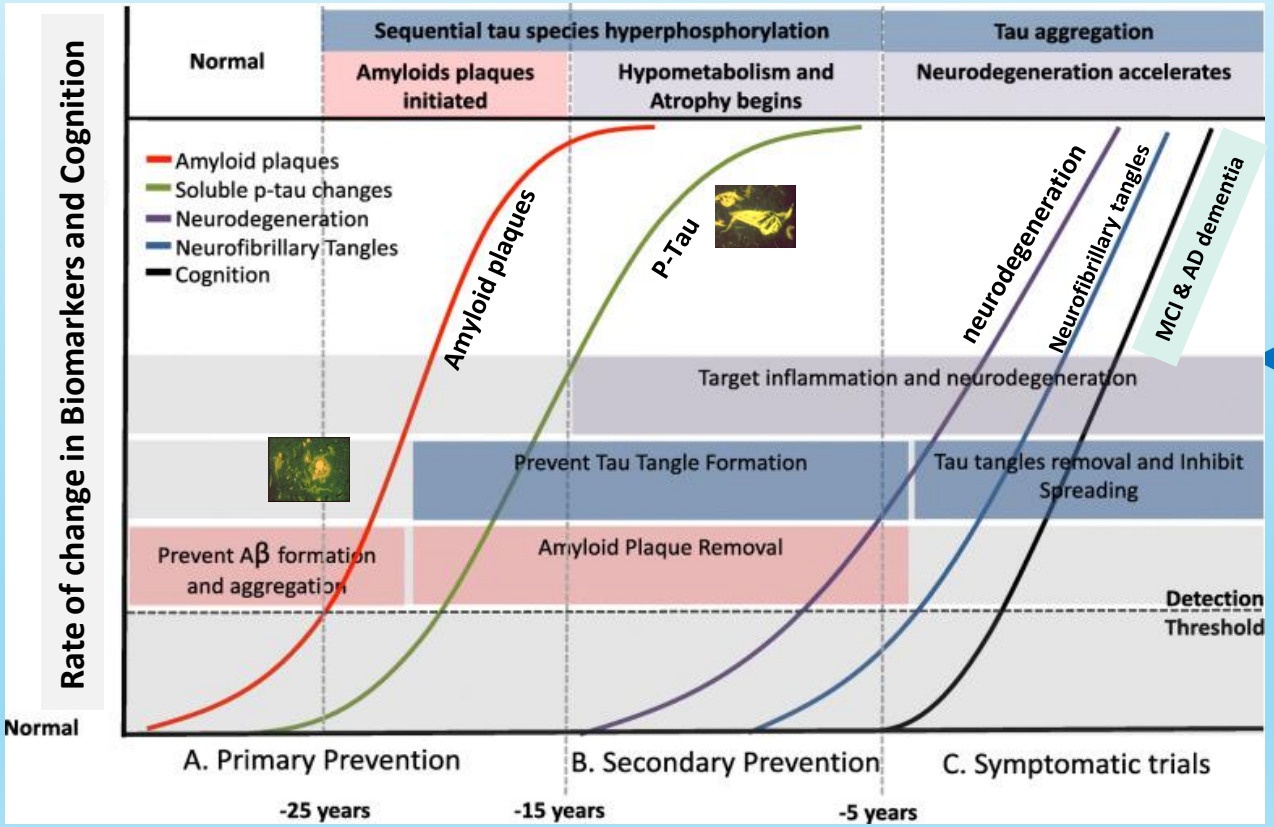
- **Alzheimer's:** 50-80%; Plaques (beta-amyloid) & Tangles (tau);
- **Vascular:** 20-40%; stroke or injury to small vessels;
  deep white matter changes, in the connecting "wires" among brain regions
- **Lewy Body:** 10-25%; alpha-synuclein deposits; hallucinations
- **Frontotemporal:** 10-15%, younger age (60% are btw 45-64 yrs)
- **Parkinson:** 50-80% of Parkinson patients eventually have dementia
- **LATE-**Limbic-predominant age-related TDP-43 encephalopathy: 20-50% >80 yrs

Mixed dementia: very common, > 50% (Alzheimer's, Vascular, Lewy Body)

Compton et al., 2022

Alzheimer's Disease: Amyloid and Tau accumulate in the brain >25 years before symptoms appear

Biomarkers to identify patients and track progress



The question is not, whether or not to intervene –

The question is, when should we intervene?

Adapted from McDade et al, 2021

Biomarker Classification

Biomarker category	fluid	imaging
Core Biomarkers		
A (Ab proteinopathy)	Ab42/40	Amyloid PET
T (AD tau proteinopathy)	ptau 181, 217	Tau PET
Non - specific biomarkers of tissue reaction involved in AD pathophysiology		
N (injury, dysfunction, or degeneration of neuropil)	NfL	Anatomic MR, FDG PET
I (inflammation) Astrocytic activation	GFAP	
Biomarkers of non-AD co-pathology		
V vascular brain injury		Anatomic infarction, WMH, abundant dilated perivascular spaces
S α-synuclein	αSyn-SAA*	

If a fluid biomarker is informative only when measured in CSF this is denoted by (*), if informative with plasma or CSF then no specific notation added.

PET and Fluid Biomarkers

Description of Initial, Early, Intermediate, and Advanced stage PET and fluid biomarkers

	Initial stage biomarkers	Early stage biomarkers	Intermediate stage biomarkers	Advanced stage biomarkers
	(a)	(b)	(c)	(d)
PET staging	amyloid PET	tau PET medial temporal region	tau PET moderate neocortical uptake	tau PET high neocortical uptake
	A+T-	$A+T_{MTL}+$	$A+T_{MOD}+$	$A+T_{HIGH}+$
Fluid staging	Ab42/40, ptau 181, 217, 231	ptauT205	MTBR-243*	Non phosphorylated tau*

PET and fluid measures are not equivalent and hence stages a-d with PET are not equivalent to stages a-d for fluid biomarkers. Nonetheless, a sequence of events exists within fluid measures and within PET in the natural history of the disease, and this is the basis for staging within PET and within fluid biomarkers.

If PET and fluid measures are available, then the most advanced biomarker stage (PET or Fluid) is used for biological staging.

Lecanemab: Appropriate use indications

Lecaneb may slow decline by 27% (5.1 months) over 18 months

Mild cognitive impairment (MCI) due to AD (intermediate likelihood)	• Cognitive concerns by the patient, knowledgeable informant, or the physician • Objective impairment in one or more cognitive domains including memory, executive function, attention, language, and visuospatial skills. • Generally preserved activities of daily living • No dementia • Positive AD biomarker
Probable AD dementia with evidence of the AD pathophysiological process	• Meets criteria for dementia • History of worsening of cognition by report or observation • The initial and most prominent cognitive deficits are evident on history and examination in one of the following categories: - Amnestic presentation - Nonamnestic presentations associated with amyloid positive confirmation • Positive amyloid biomarker
Cognitive impairment severity	• MMSE score of 22-30 to define MCI and mild AD dementia

All patients will be enrolled in a registry like the CMS or Alzheimer's Network for Treatment and Diagnostics (ALZ-NET) for post-marketing surveillance; Patients receive IV infusions every 2 weeks.

VanDyck et al., 2023; Cummings et al. J Prev Alz Dis 2023

Donanemab: TRAILBLAZER-ALZ2 trial, randomized, double-blind

- **TRAILBLAZER-ALZ2 trial met all of its primary and secondary endpoints. Nearly half (47%) of participants taking donanemab had no decline of cognition and function for one year (vs 29% on placebo).**

- **Donanemab slowed clinical decline by 35% compared to placebo on the primary outcome measure.**

- **Donanemab resulted in 40% less decline in the ability to perform activities of daily living, such as managing finances, driving, engaging in hobbies, and conversing about current events.**

- **Given every 4 week, by infusion over 30 min; MMSE: 20-28.**

S.E. -- ARIA-E occurred in 24.0% of treated participants, with 6.1% experiencing symptomatic ARIA-E. ARIA-H occurred in 31.4% in the donanemab group and 13.6% in the placebo group

J Sims et al. JAMA, 2023

Alzheimer's disease and eligibility for Lecanemab can be determined

- An appointment can be made at UAMS with Dr. Gohar Azhar at the Longevity Clinic, Walker Memory Center;

- A comprehensive memory evaluation will be performed;

- Other tests will include:
  lab tests specific for memory disorders
  A baseline MRI
  A spinal tap for beta amyloid and pTau; if this is positive, it will confirm Alzheimer's disease;

- Then one could be eligible for lecanemab if criteria are met.

Cognitive Resilience strategies

- Exercise, lifestyle, hearing
- Being present in the moment
- Social intelligence and awareness
- Environmental factors, prevent head trauma
- Additional learning;
  Mind-challenging opportunities
- Genetic factors
- Friends and family connections
- Resilience training; humor & curiosity
- New and future therapies