Adapting a Neurocognitive Clinic in the Era of Anti-Amyloid Therapy

The Good, The Bad, and Ugly Uncertainty

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Ochsner Health

Presenter Disclosure

- I have no current or past relationships with commercial entities.
- Potential for conflict(s) of interest: None

Commercial Support Disclosure

- To the presenter knowledge, this program has received no financial or in-kind support from any commercial or other organization.
- Potential for conflict(s) of interest: None

A Paradigm Shift

- **Historically Behavioral/Cognitive Neurology was the quintessential armchair discipline**
  - Clinic-based, episodic evaluation, and limited therapeutic consequence

- Between 2022-2026 the subspeciality has become
  - **Data-driven**
  - **Operational**
  - **Interventional**
  - **Continuous**

- **What changed**
  - Biology is directly measurable
  - Disease-modifying therapies
  - Time-sensitive clinical decisions

Patients expect and demand—<u>active</u> intervention

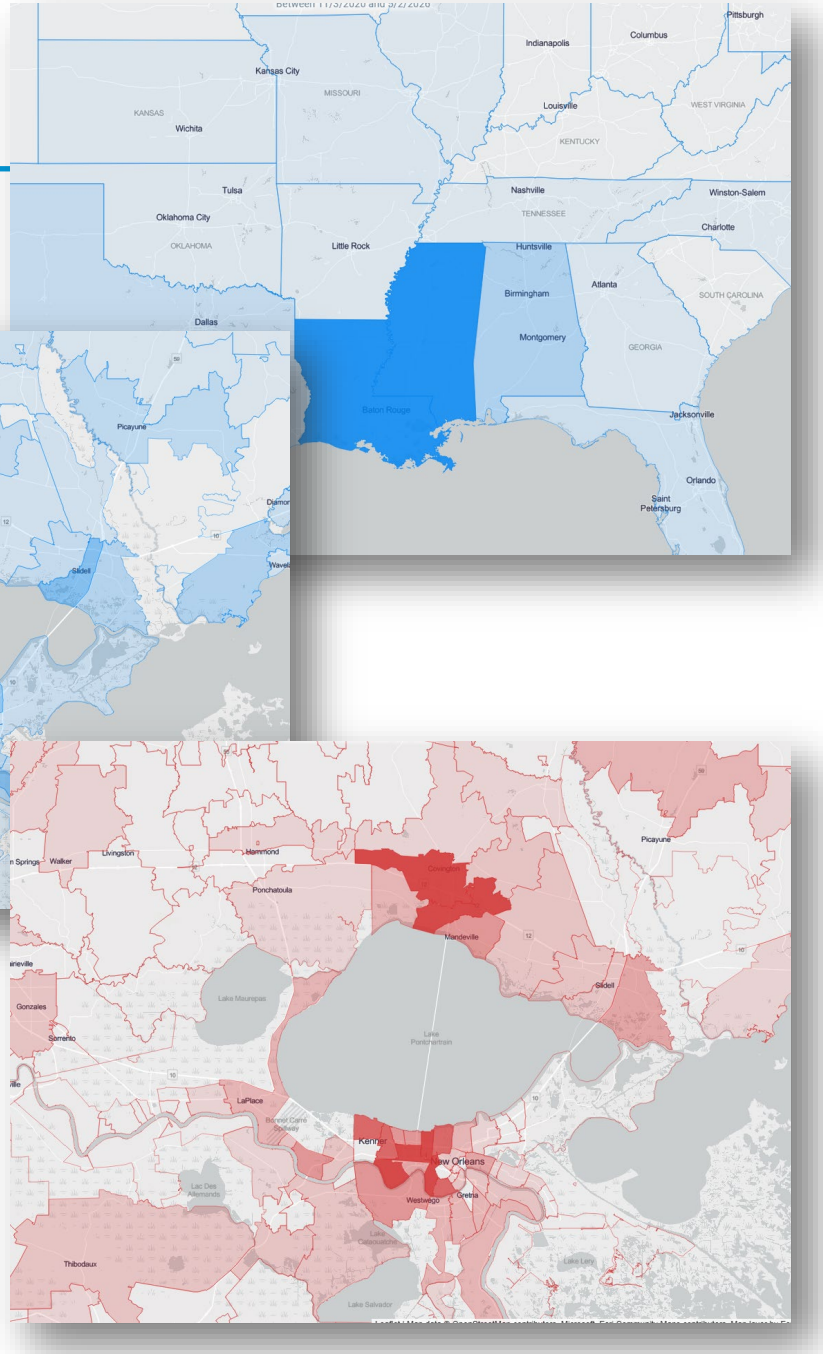
Open Frontier of Neurology

- **Ochsner Neurocognitive Program 2022-2026**
  - Regional Neurocognitive Center of Louisiana
  - Neurocognitive **Hub for the Gulf South**
    - 2 Behavioral Neurologists
    - 1 Vascular Cognitive Neurologist
    - 5 Advanced practice providers
  - Comparable in size to UAB/Emory ***but***
    - Longitudinal care model
    - Advanced Therapeutic Access
    - Multidisciplinary network of providers

- **Today we share our experience…**
  - What we expected
  - What we observed
  - What it cost us to see it

Open Frontier of Neurology

- **Catchment Expansion**
  - Geographic spread ↑
    - 15 States
  - Referral density ↑
    - #1 Referral center in LA for neurocognitive disorders



- **Clinic Population Growth**
  - Unique patients ↑ >2500 patients
  - AAT patients ↑ >250 patients
    - Monitoring volume ↑
    - Biomarker tracking ↑

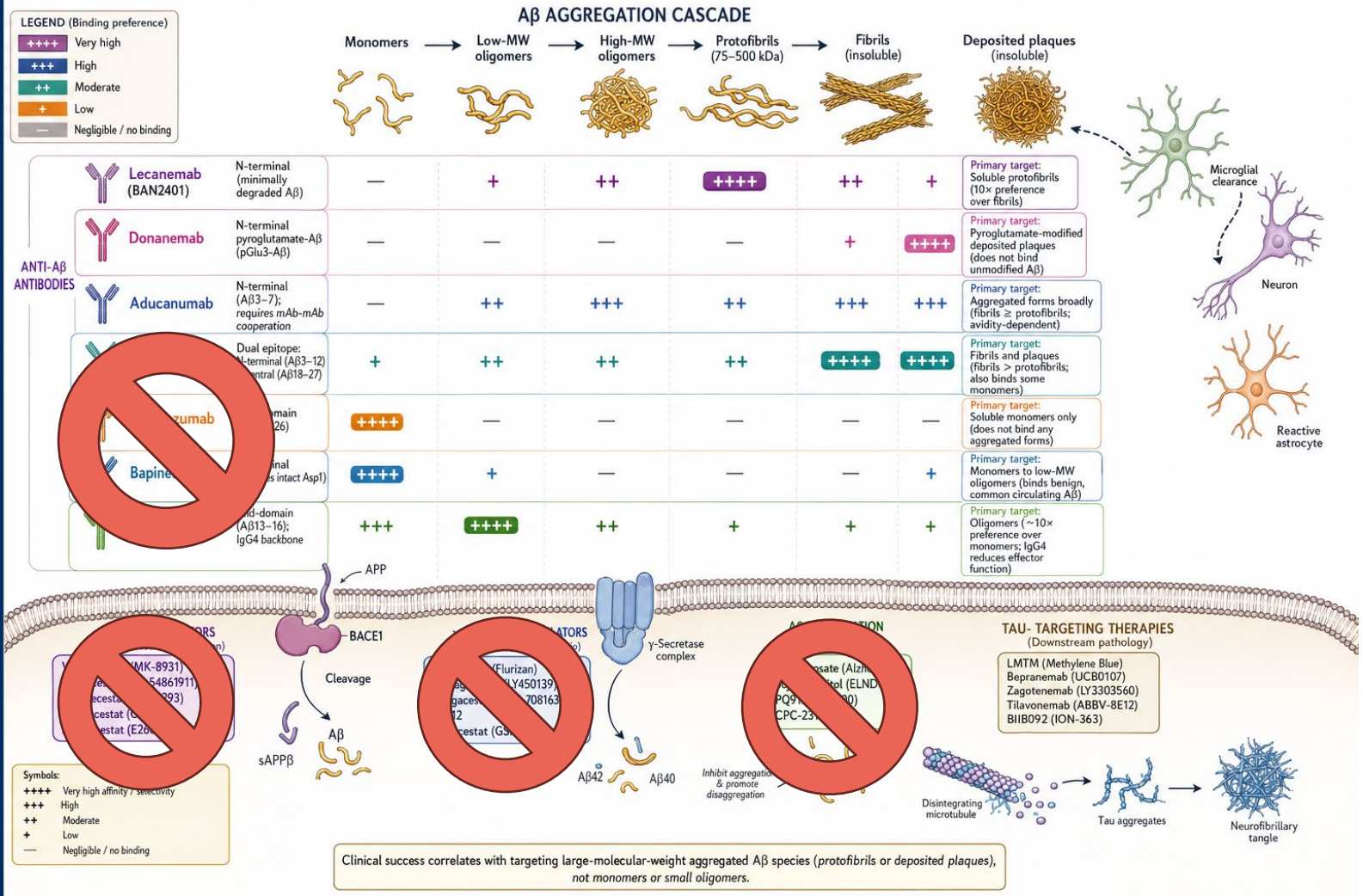
ANTI-AMYLOID THERAPY

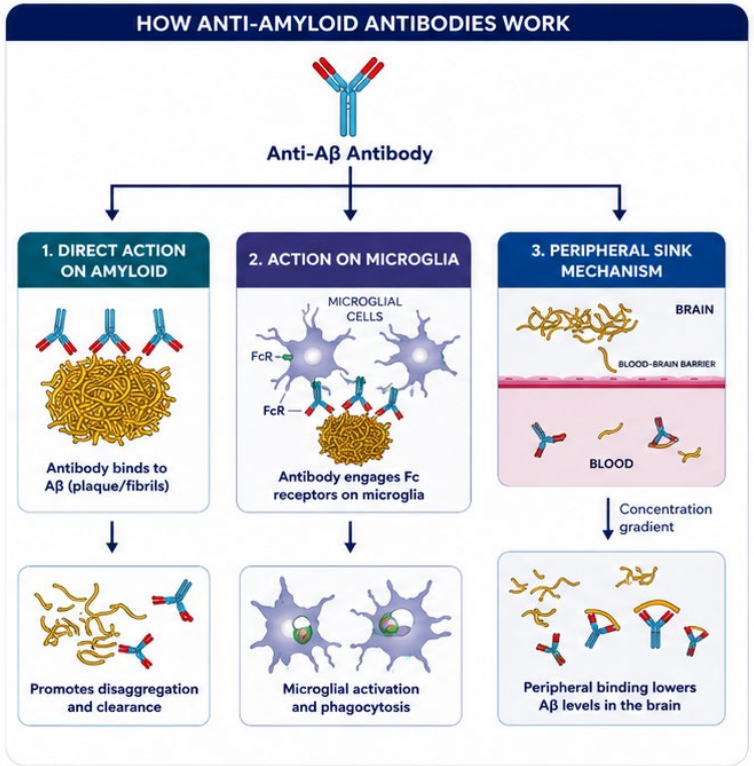
★ TRANSITION INTO THE CLINIC ★

★ LITERATURE AND CLINICAL DATA ★

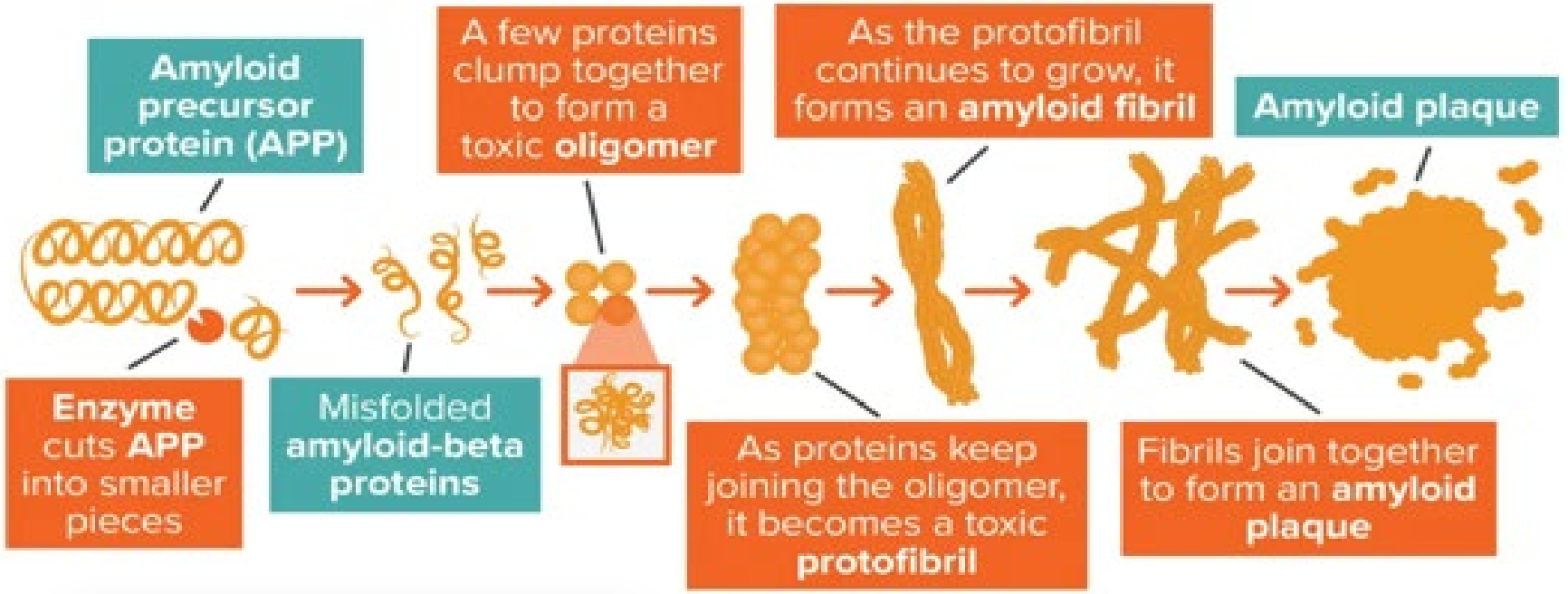
Ochsner Health

What is Anti-Amyloid Therapy





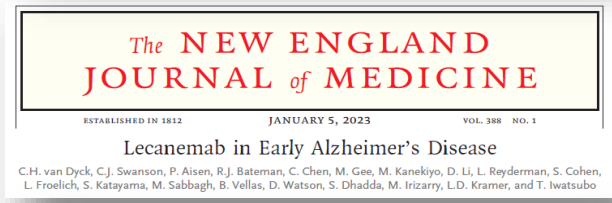
Luna-Muñoz et al., 2013; Olsson et al., 2016; Panza et al 2019; Hansson., 2021



JAMA | Original Investigation

Donanemab in Early Symptomatic Alzheimer Disease
The TRAILBLAZER-ALZ 2 Randomized Clinical Trial

John R. Sims, MD; Jennifer A. Zimmer, MD; Cynthia D. Evans, PhD; Ming Lu, MD, MS, MPH; Paul Ardayfio, PhD; JonDavid Sparks, PhD; Alette M. Wessels, PhD; Sergey Shcherbinin, PhD; Hong Wang, PhD; Emel Serap Monkul Nery, MD; Emily C. Collins, PhD; Paul Solomon, PhD; Stephen Salloway, MD; Liana G. Apostolova, MD; Oskar Hansson, MD, PhD; Craig Ritchie, MD, PhD; Dawn A. Brooks, PhD; Mark Mintun, MD; Daniel M. Skovronsky, MD, PhD; for the TRAILBLAZER-ALZ 2 Investigators

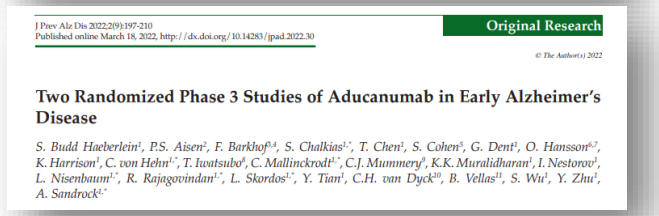


The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 5, 2023 VOL. 388 NO. 1

Lecanemab in Early Alzheimer's Disease

C.H. van Dyck, C.J. Swanson, P. Aisen, R.J. Bateman, C. Chen, M. Gee, M. Kanekiyo, D. Li, L. Reyderman, S. Cohen, L. Froelich, S. Katayama, M. Sabbagh, B. Vellas, D. Watson, S. Dhadda, M. Irizarry, L.D. Kramer, and T. Iwatsubo



J Prev Alz Dis 2022;2(9):197-210
Published online March 18, 2022, http://dx.doi.org/10.14283/jpad.2022.30

Original Research

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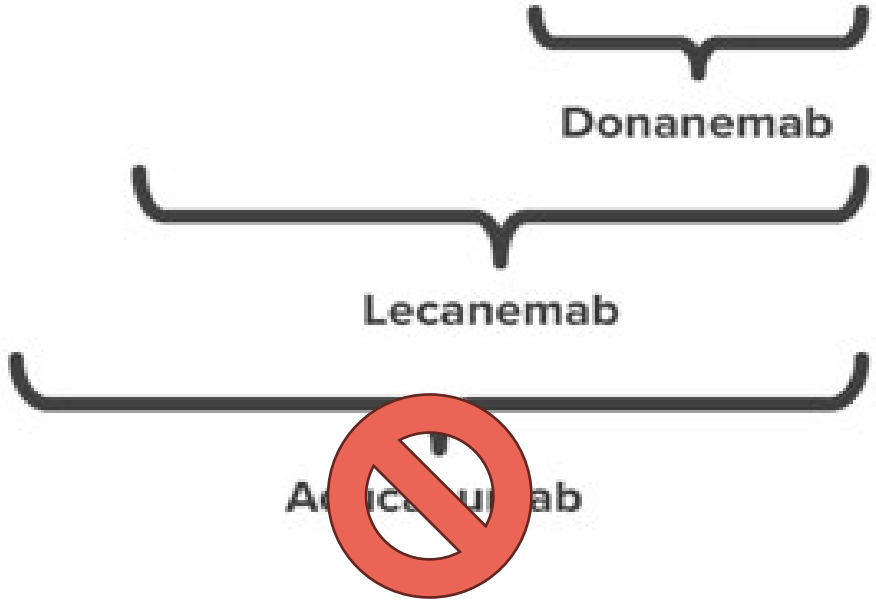
Two Randomized Phase 3 Studies of Aducanumab in Early Alzheimer's Disease

S. Budd Haeberlein[1], P.S. Aisen[2], F. Barkhof[3,4], S. Chalkias[1,*], T. Chen[1], S. Cohen[5], G. Dent[1], O. Hansson[6,7], K. Harrison[1], C. von Hehn[1,*], T. Iwatsubo[8], C. Mallinckrodt[1,*], C.J. Mummery[9], K.K. Muralidharan[1], I. Nestorov[1], L. Nisenbaum[1,*], R. Rajagovindan[1,*], L. Skordos[1,*], Y. Tian[1], C.H. van Dyck[10], B. Vellas[11], S. Wu[1], Y. Zhu[1], A. Sandrock[1,*]



Aducanumab
- Published 2016
- FDA **approval 2021**
- CMS coverage 2022
  - ***Restricted***
- Withdrawn 2024

Lecanemab:
- Published 2022
- FDA/CMS **approval 2023**

Donanemab:
- Published 2023
- FDA/CMS **approval 2024**

What the Trials Actually Showed

Relevant End Points

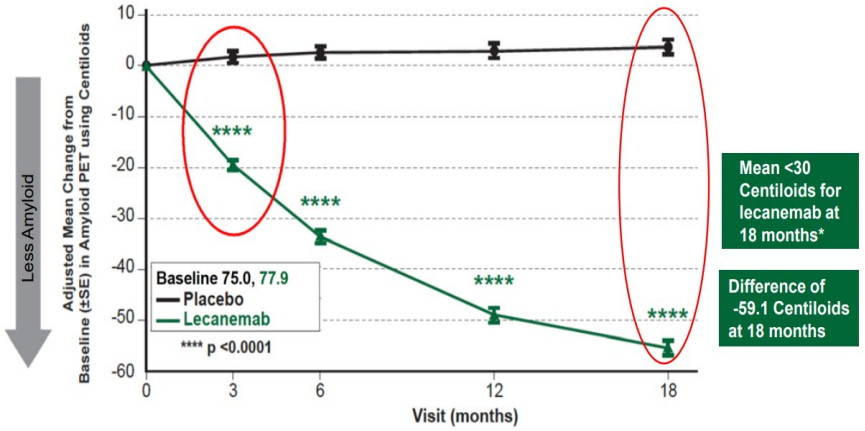
1. Amyloid Reduction
2. Tau Reduction
3. Clinical Decline Slowing
4. Safety

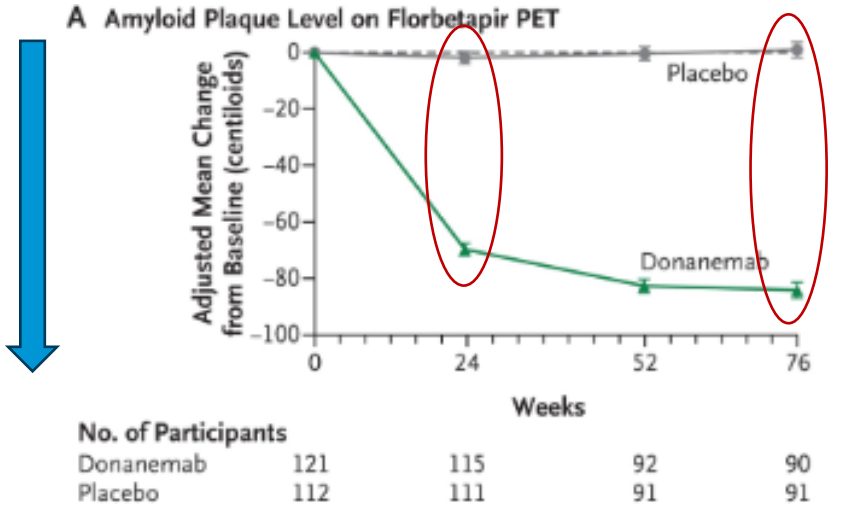
Parameter	CLARITY AD (Lecanemab)	TRAILBLAZER-ALZ 2 (Donanemab)
Trial Phase	Phase 3	Phase 3
N (total)	1,795	1,736
MMSE Eligibility Range	22–30	20–28
Mean MMSE — Treatment Arm	25.5 ± 2.2	22.52 ± 3.84 (combined tau)
Mean MMSE — Placebo Arm	25.6 ± 2.2	22.20 ± 3.90 (combined tau)
Mean MMSE — Low/Med Tau (Treatment)	N/A (no tau stratification)	23.11 ± 3.64
Mean MMSE — Low/Med Tau (Placebo)	N/A (no tau stratification)	22.88 ± 3.74
Classification Method	CDR-Global (0.5 vs 1.0)	MMSE score bands
MCI (%)	61.5% (CDR 0.5)	~17% (MMSE ≥27)
Mild AD (%)	38.5% (CDR 1.0)	~83% (MMSE 20–26)
Baseline SD Spread	Narrow (±2.2)	Wide (±3.8–3.9)
Population Severity	**Less impaired**	**More impaired**

Shcherbinin et al., 2022; van Dyck et al., 2023; Sims et al., 2023; Lu et al., 2025; van Dyck et al., 2025; Fox et al., 2025

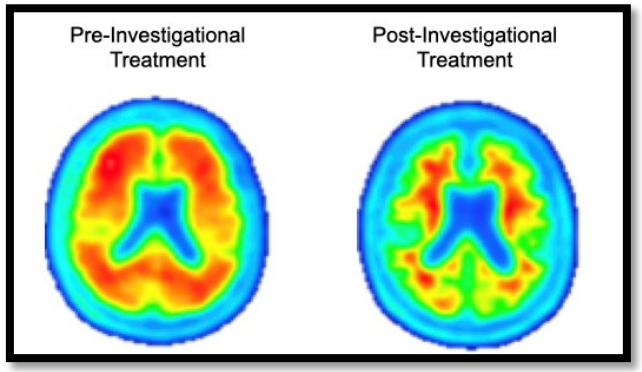
What the Trials Actually Showed: *Amyloid*

- **Lecanemab (CLARITY AD, N = 1,795):**
  - Approx 59.1 centiloid reduction at 18m
    - 68% amyloid-negative status (<30 centiloids)
- **Donanemab (TRAILBLAZER-ALZ 2, N = 1,736):**
  - Approx. 88 centiloid reduction at 19m
    - 80% amyloid-negative status (<25 centiloids)





After 18 months of anti-amyloid infusions



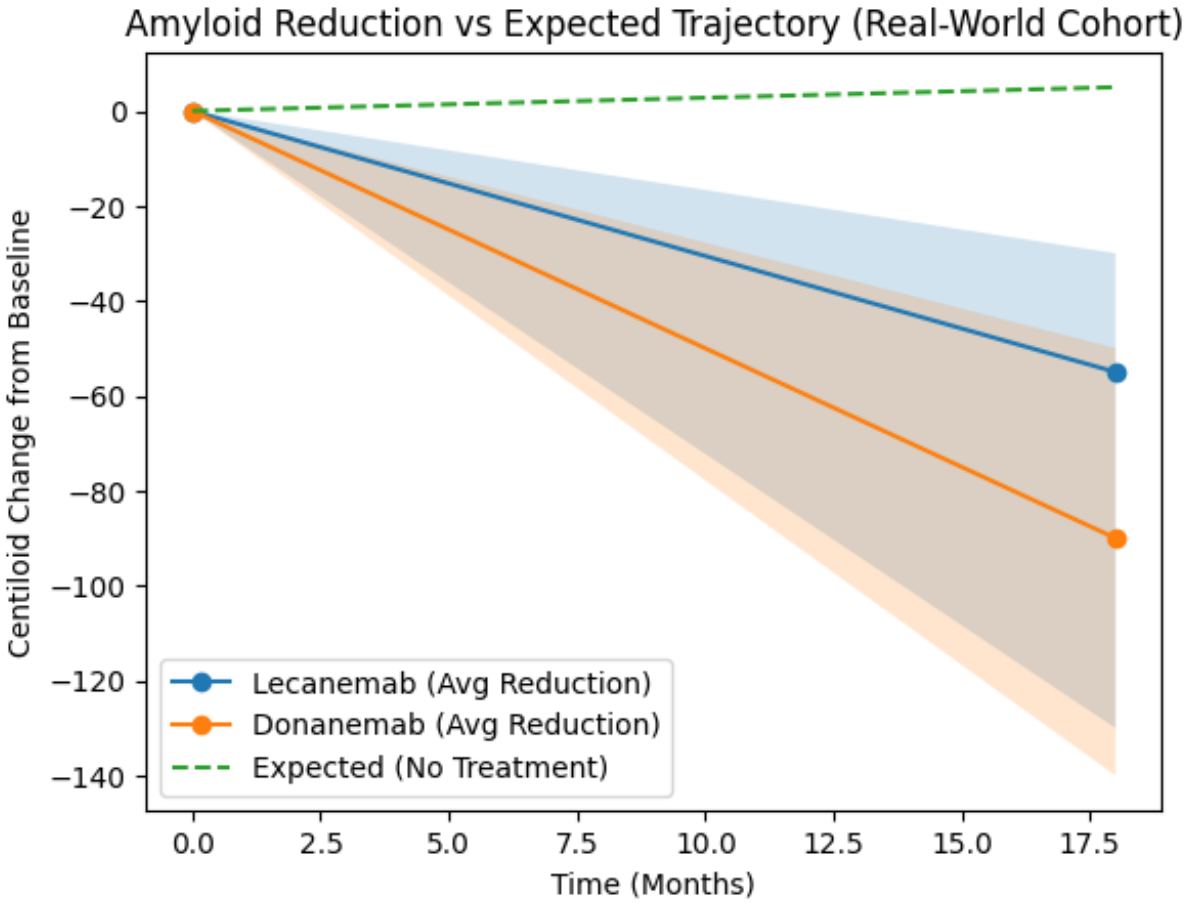
Shcherbinin et al., 2022; van Dyck et al., 2023; Sims et al., 2023; Lu et al., 2025; van Dyck et al., 2025; Fox et al., 2025

Real-World Clinic Data: ***Amyloid***

- **Expected Effect (Confirmed)**
  - Lecanemab: ~50–60 CL ↓
  - Donanemab: ~80–90 CL ↓
  - Subset normalize (<25 CL)

- **Observed Response Patterns**
  - **Primary factor determining normalization is baseline PET**
  - **Early disease (baseline <50 CL)**
    - Most robust responders
    - Frequently ↓ to negative range (≈ –10 to –20 CL)
  - **High-burden patients**
    - Larger absolute reductions but remain persistently positive
    - **Poor Responders (Emerging Phenotype)**
      - Genetic carriers (PSEN1, POLG, GBA1, ETC.)

- **Augmented Responders**
  - Prior exposure:
    - Clinical trials
    - Other disease-modifying therapies
  - Suggests:
    - "Primed" biological system for clearance kinetics

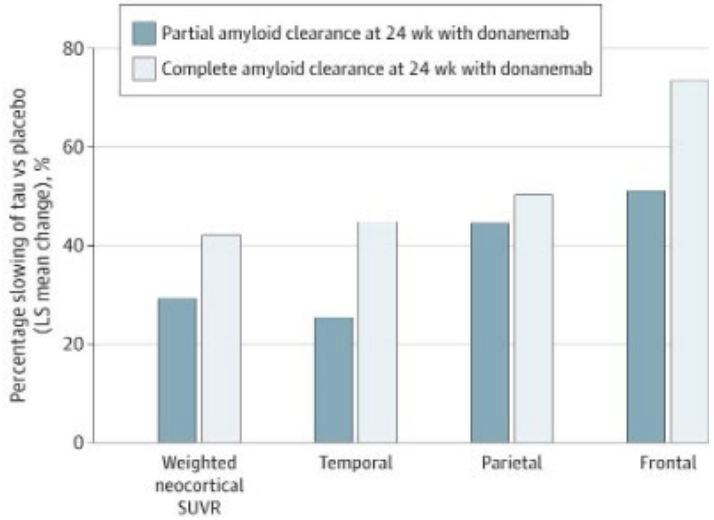


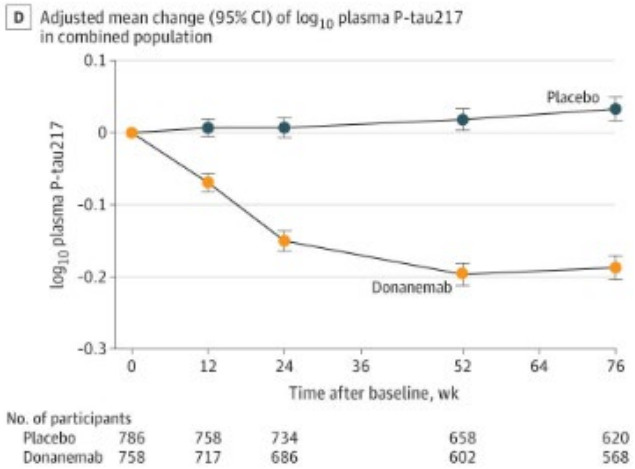
Amyloid clearance is consistent— but response is biologically stratified

What the Trials Actually Showed: *Tau*

- **Donanemab**
  - **Tau PET:**
    - Phase 2 trial: 34% slowing of tau **BUT** Region-dependent:
      - **Significant slowing**: Parietal and frontal
      - **Not significant**: Global, Temporal inferior
    - Phase 3 trial: ***not significant***
  - **Plasma p-tau217:**
    - **23% reduction** (P<0.001)
      - Persisted up to **1 year after treatment**
      - Correlated with amyloid reduction (P<0.001)

- **Lecanemab**
  - **Tau PET:**
    - **Significant slowing**: medial temporal (P<0.01), temporal (P<0.05)
    - **Not significant** : Global, frontal, cingulate, parietal, occipital
  - **Plasma p-tau181** ***derived estimates, not published***
    - Phase 2: **26% reduction** (P<0.0001)
    - Phase 3: **21% reduction** (P<0.0001)



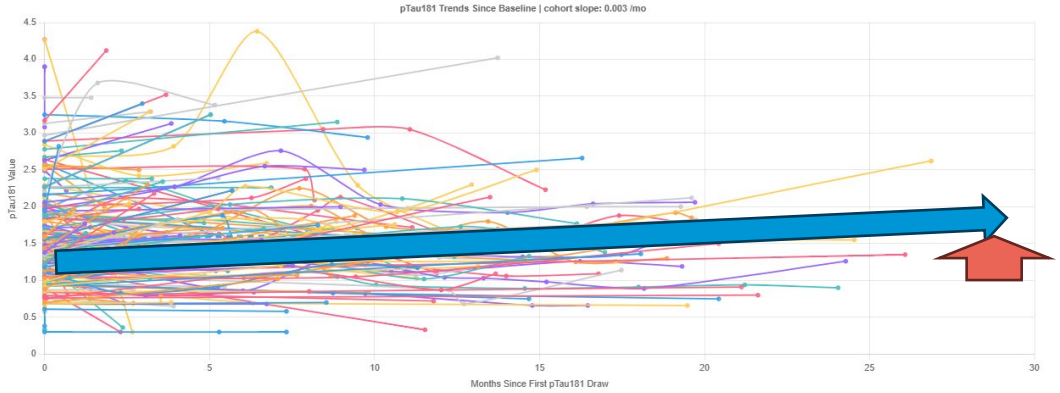


Shcherbinin et al., 2022; van Dyck et al., 2023; Sims et al., 2023; Lu et al., 2025; van Dyck et al., 2025; Fox et al., 2025

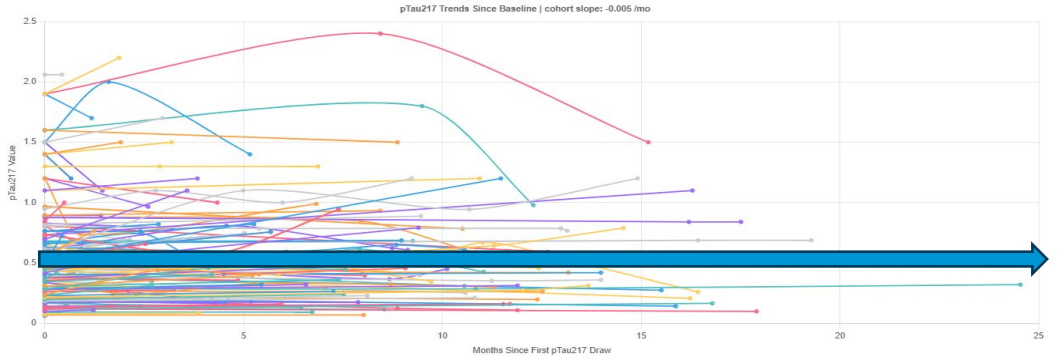
Real-World Clinic Data: ***Tau***

- What we have seen in our Alzheimer patients who have **not** been on AAT
  - Minor gradual rise of serum p-tau181
  - Largely stable serum p-tau217
  - Significant consistent rises in GFAP>Nfl
  - **Not uniform:** stage of disease, age, drivers, comorbidities

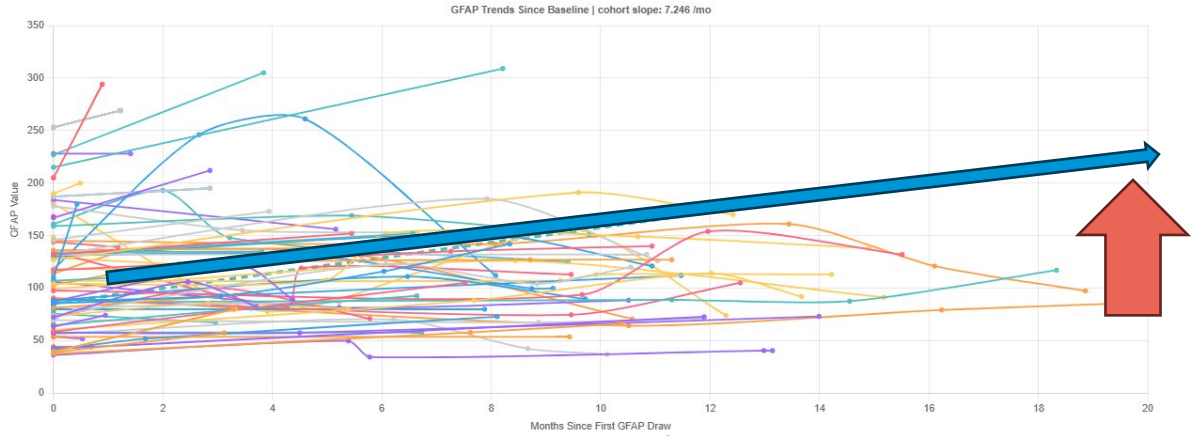
pTau181 (Test ID 61)



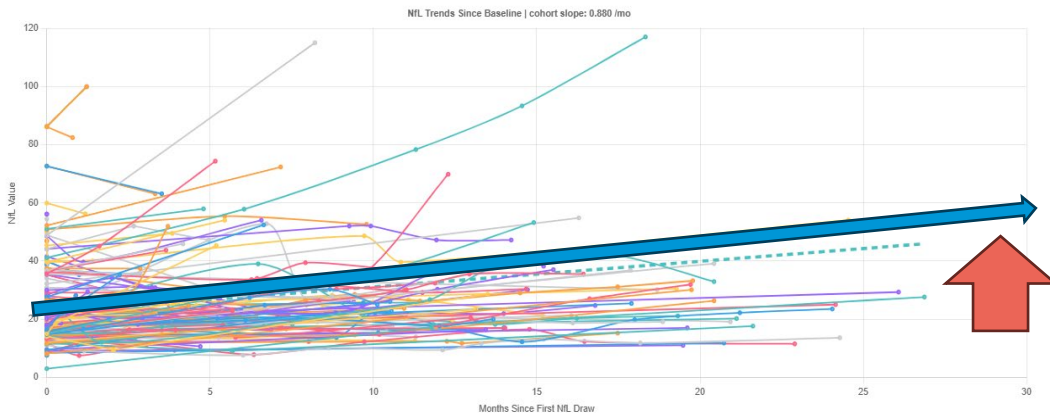
pTau217 (Test ID 205)



GFAP (Test IDs 656 / 1322)



NfL (Test ID 67)

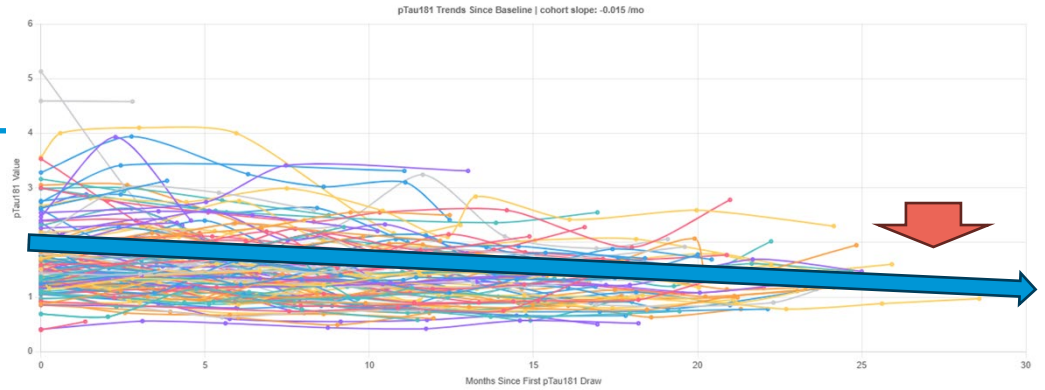


Patient with spikes due to identifiable causes (head trauma, surgeries, infections, etc.) removed from graphs

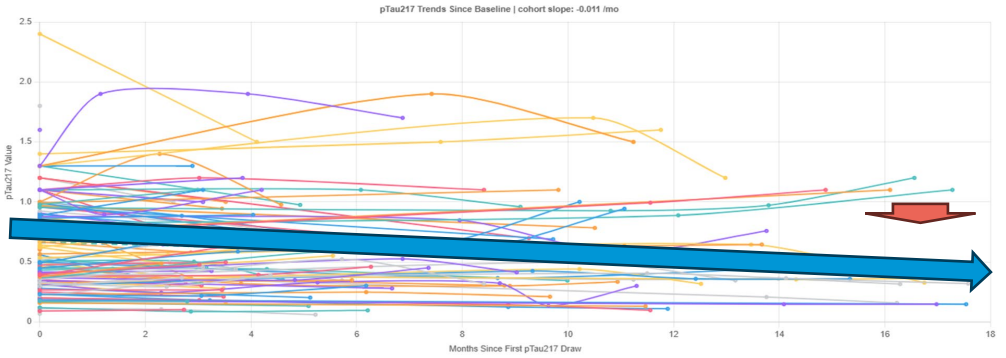
Real-World Clinic Data: ***Tau***

- What we have seen in our Alzheimer patients who ***are*** on AAT
  - Modest consistent decrease of serum p-tau181
  - Borderline but consistent decrease serum p-tau217
  - *Expected* Nfl monthly rise ***slowed by 3.0x***
  - *Expected* GFAP monthly rise ***slowed by 5.1x***
  - **Not uniform:** stage, age, drivers, comorbidities

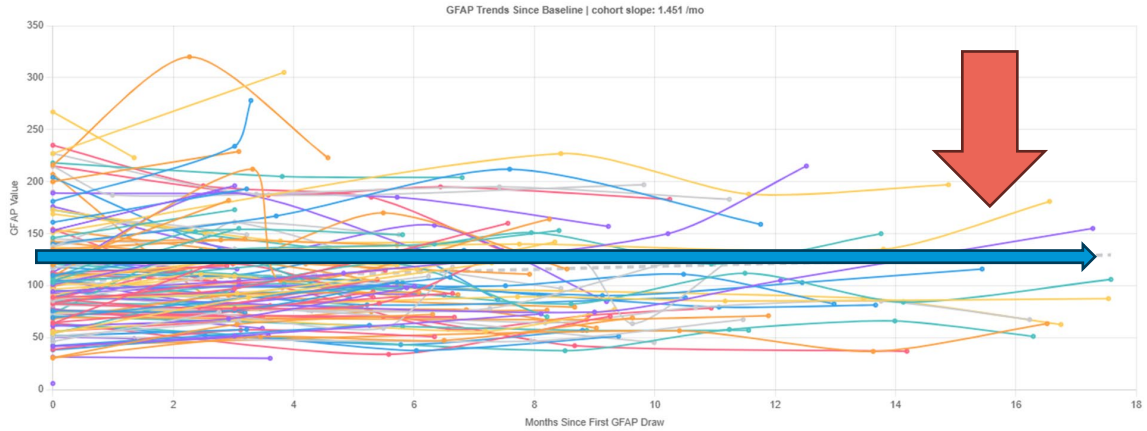
pTau181 (Test ID 61)



pTau217 (Test ID 205)



GFAP (Test IDs 656 / 1322)



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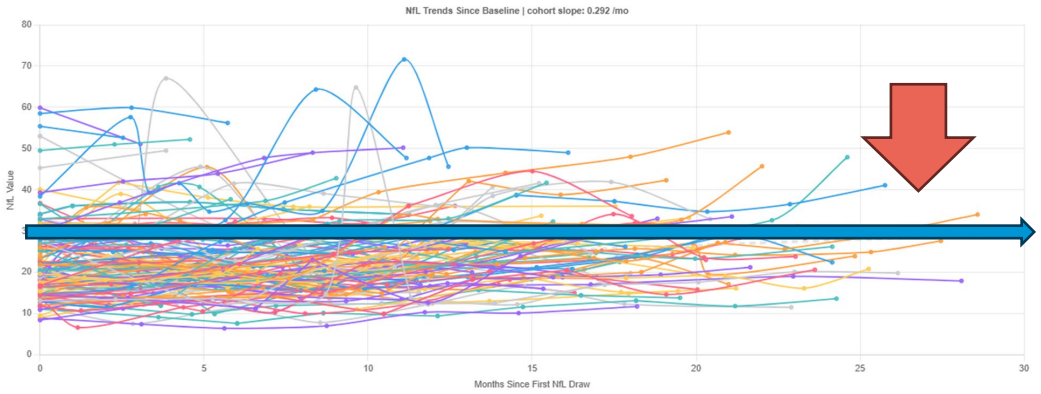


*****Patient with spikes due to identifiable causes (head trauma, surgeries, infections, etc.) removed from graphs*****

What the Trials Actually Showed: *Clinical*

Anti-amyloid therapy slows decline — it does not reverse it.

LECANEMAB

CLARITY-AD

Primary endpoint
CDR-SB at 18 months

27%
relative slowing
(P = 0.001)

ADAS-Cog14 at 18 months
26%
relative slowing
(P = 0.001)

Separation from placebo emerged progressively over 18 months

Demonstrated consistent but modest slowing of decline.

DONANEMAB

TRAILBLAZER-ALZ 2

Primary endpoint
CDR-SB

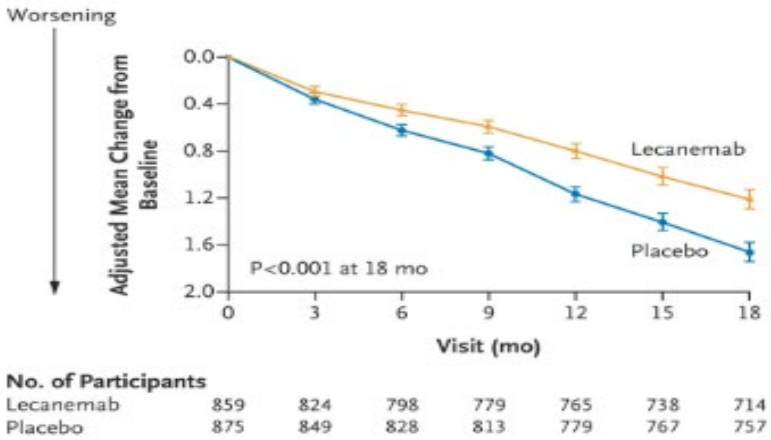
29–36%
relative slowing
(P = 0.001)

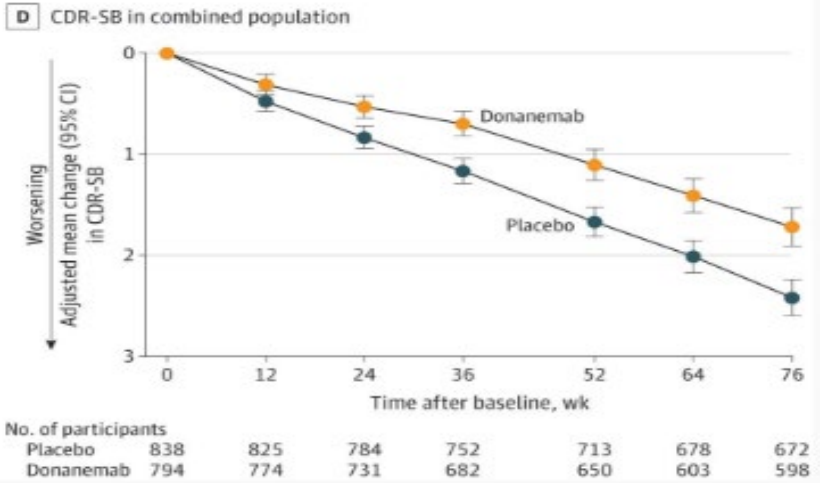
- Low/intermediate tau: **36%**
- Combined population: **29%**

iADRS (low/intermediate tau)
35%
relative slowing
(P = 0.001)

iADRS (combined population)
22%
relative slowing
(P = 0.001)

Suggested stronger effect in selectively enriched populations.





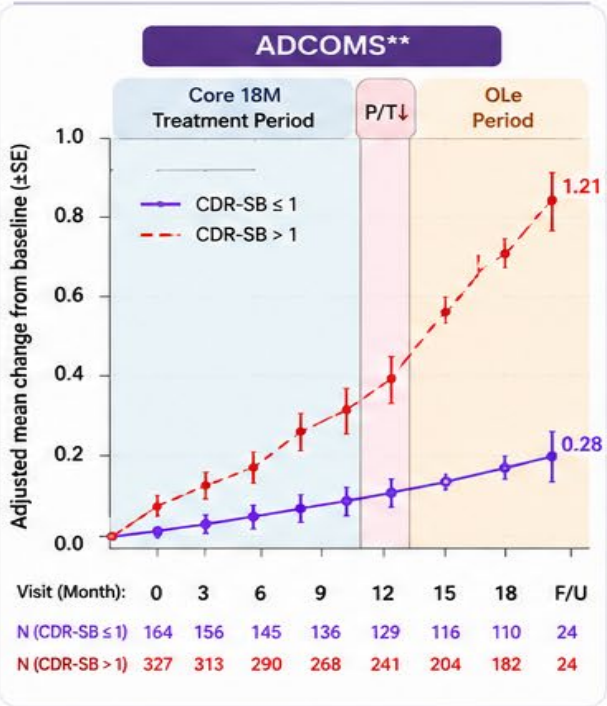
Shcherbinin et al., 2022; van Dyck et al., 2023; Sims et al., 2023; Lu et al., 2025; van Dyck et al., 2025; Fox et al., 2025

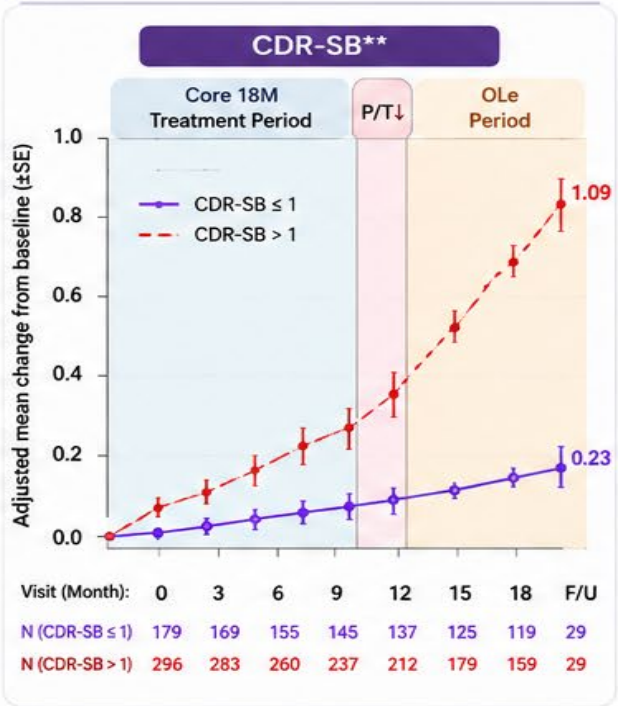
What the Trials Actually Showed: *Clinical*

The dominant variable is ***not*** exposure to drug—
it is disease stage at the time of exposure.

- Early treatment → alters trajectory
- Late treatment → attenuated effect
- Delayed treatment → cannot "catch up"

LECANEMAB





DONANEMAB

- **CDR-SB**
  - MCI: **46%**
  - Dementia: **38%**
- **iADRS:**
  - MCI: **60%**
  - Dementia: **30%**

Percent slowing vs. placebo over 76 weeks

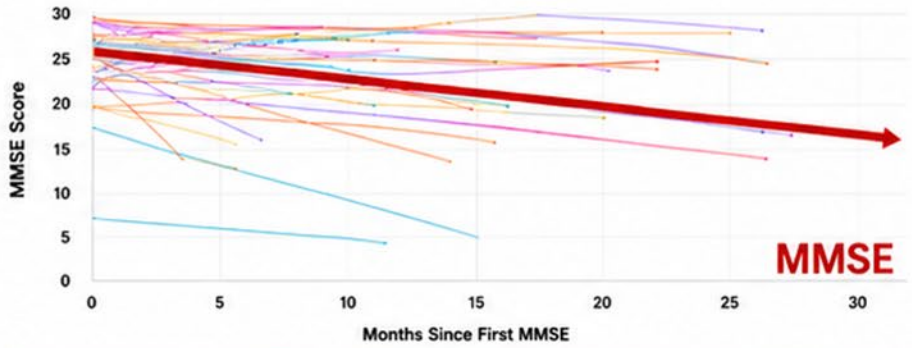
This is a strong **stage-dependent** treatment effect for both medications.

Swanson et al., 2021; Shcherbinin et al., 2022; van Dyck et al., 2023; Sims et al., 2023; Lu et al., 2025; van Dyck et al., 2025; Fox et al., 2025

Real-World Clinic Data: *Clinical*

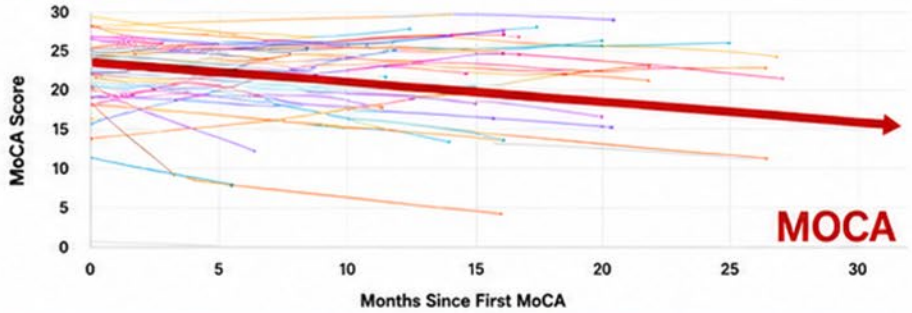
Our Alzheimer patients who are ***not*** on AAT

MMSE Over Time



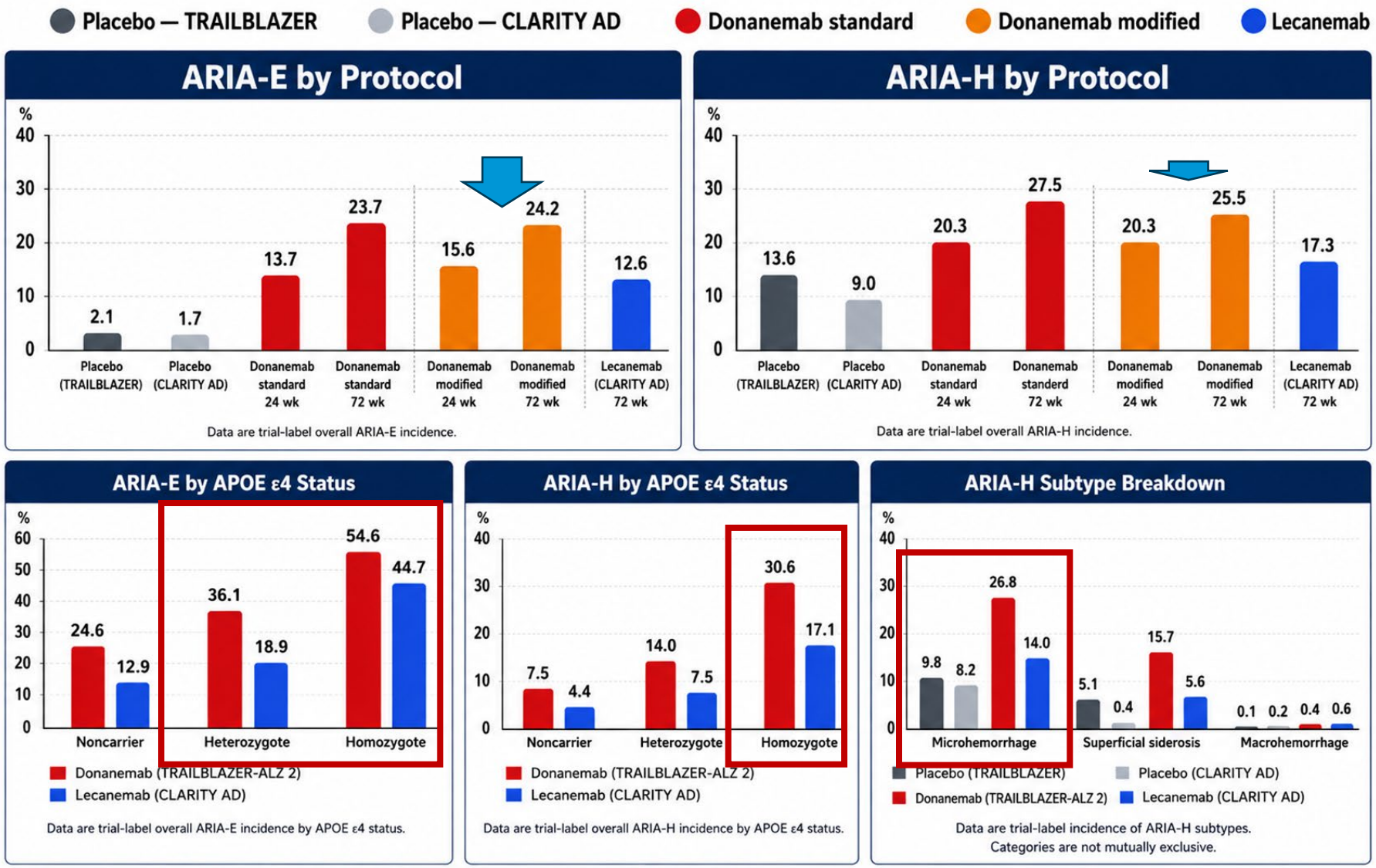
Literature: ↓ 0.14 (MCI) – 0.33 (Dementia) /monthly | **Clinic: ↓ 0.202/monthly**

MoCA Over Time



Literature: ↓ 0.05 (MCI) – 0.33 (Dementia) /monthly | **Clinic: ↓ 0.169/monthly**

What the Trials Actually Showed: *Safety*



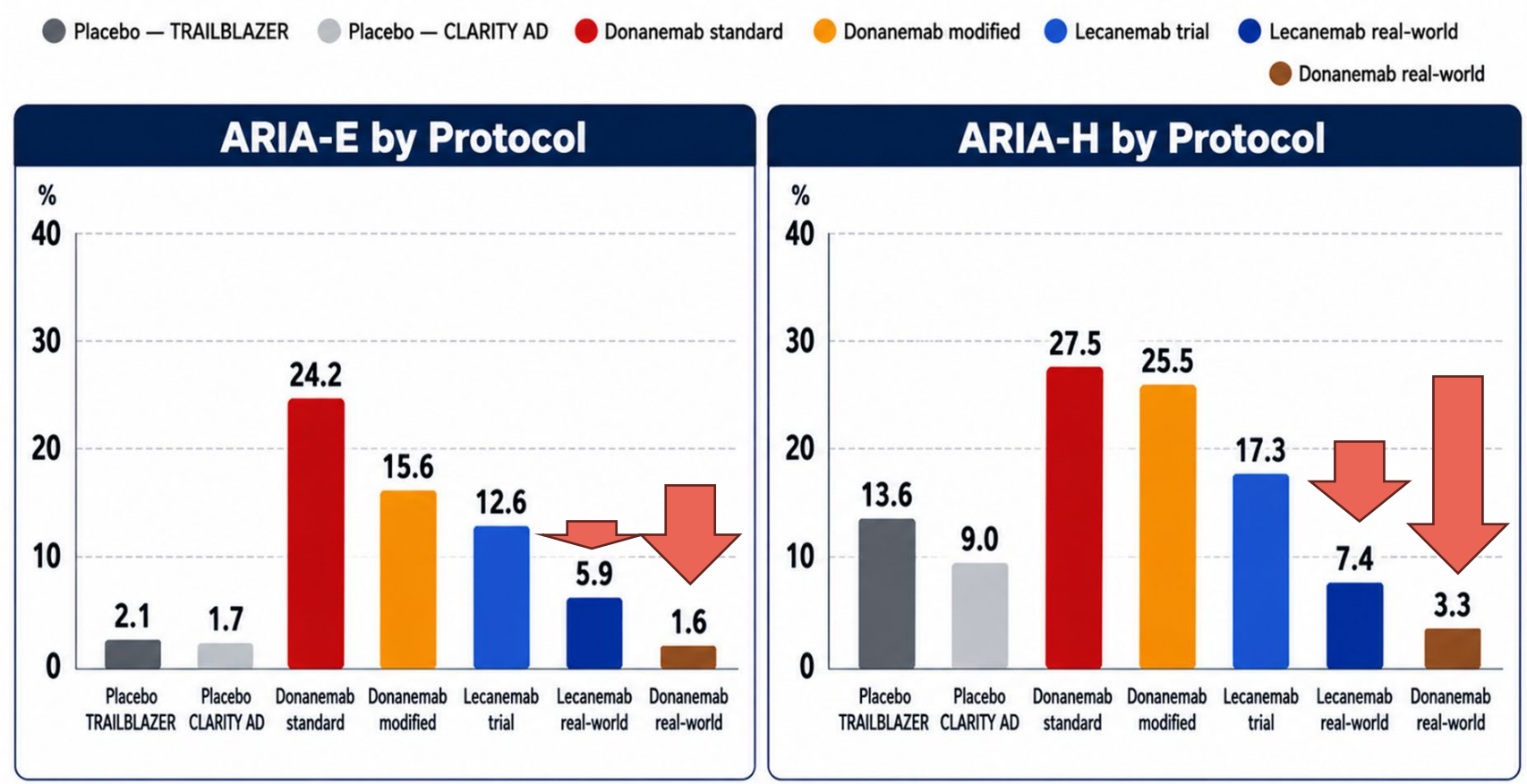
ARIA-E = amyloid-related imaging abnormality – edema/effusion; ARIA-H = amyloid-related imaging abnormality – hemosiderin deposition.
Sources: TRAILBLAZER-ALZ 2 (donanemab) Prescribing Information; CLARITY AD (lecanemab) Prescribing Information.
Note: Data reflect the highest exposure time point evaluated in each study. Donanemab standard and modified dosing include 24-week and 72-week time points.

- Modified Titration of Donanemab decreased rates of ARIA
  - ARIA-H not markedly decreased after 72 wks
- ARIA mildly influenced by E4 status
- ARIA-H markedly influenced by E4/E4
- Most ARIA-H clinically silent CMBs

Shcherbinin et al., 2022; van Dyck et al., 2023; Sims et al., 2023; Lu et al., 2025; van Dyck et al., 2025; Fox et al., 2025

Real-World Clinic Data: *Safety*

- **Observed ARIA Rates (Real-World)**
  - Lower than trial-reported rates:
    - Patient selection
    - Monitoring intensity
    - Clinical caution
- **Primary Risk Modifiers**
  - **CAA (dominant driver)**
    - Exclusion → substantial risk reduction
  - **APOE ε4 status**
    - Dose-dependent risk contribution
- **Amplifiers of Risk (Clinical Reality)**
  - Anticoagulation / vascular fragility
  - Falls, trauma, surgical stress
  - Chronic inflammatory states (autoimmune, DMARD exposure)
  - Intercurrent illness (infection)
  - COVID



Clinic data: N=264; lecanemab N=203; donanemab/Kisunla N=61; ARIA-E=13; ARIA-H=17; overlap E+H=4; no ARIA=238.

Real-world: Lecanemab 12/203 = 5.9%; Donanemab 1/61 = 1.6% | **Real-world:** Lecanemab 15/203 = 7.4%; Donanemab 2/61 = 3.3%

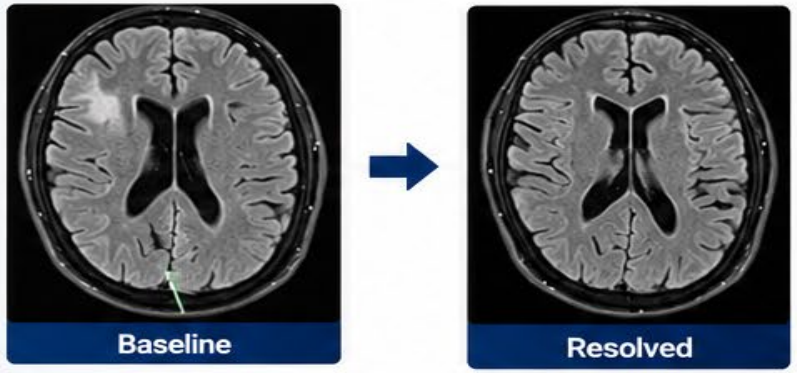
Risk is screenable —but it is not static; it is context-dependent

Real-World Clinic Data: *Safety*

Most ARIA-E and ARIA-H are mild and self-limited

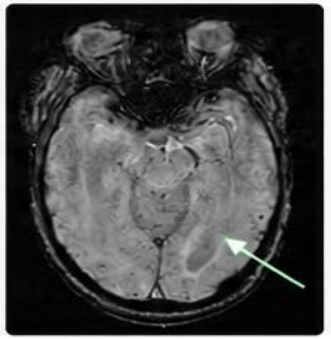
Most ARIA-E

Self resolves



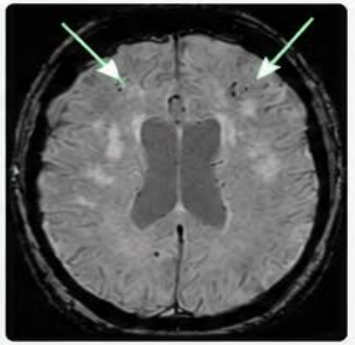
Most ARIA-H

Mild w/o SXS

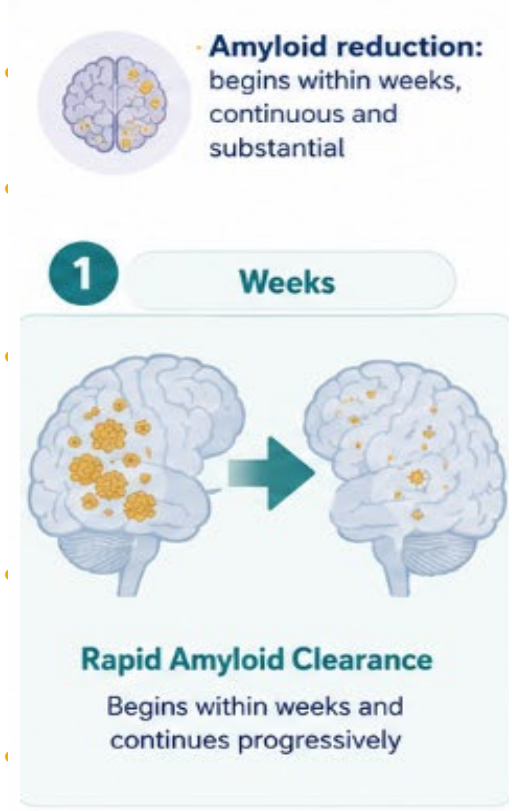


Most ARIA-H

Moderate w/o SXS



What these Medications Actually Do: ***Summary***



Shcherbinin et al., 2022; van Dyck et al., 2023; Sims et al., 2023; Lu et al., 2025; van Dyck et al., 2025; Fox et al., 2025

REAL-WORLD CLINIC EXPERIENCE

Case examples of
Good, Bad, and Uncertain

Ochsner Health

Same Drug, Same Disease — Divergent Trajectories

WHAT WE OBSERVED

THE GOOD

- Early tau reduction
- Functional stability
- Sustained biologic response

THE UNCERTAIN (UGLY)

- Persistent regional disease despite global amyloid reduction
- Ongoing focal dysfunction despite biomarker improvement

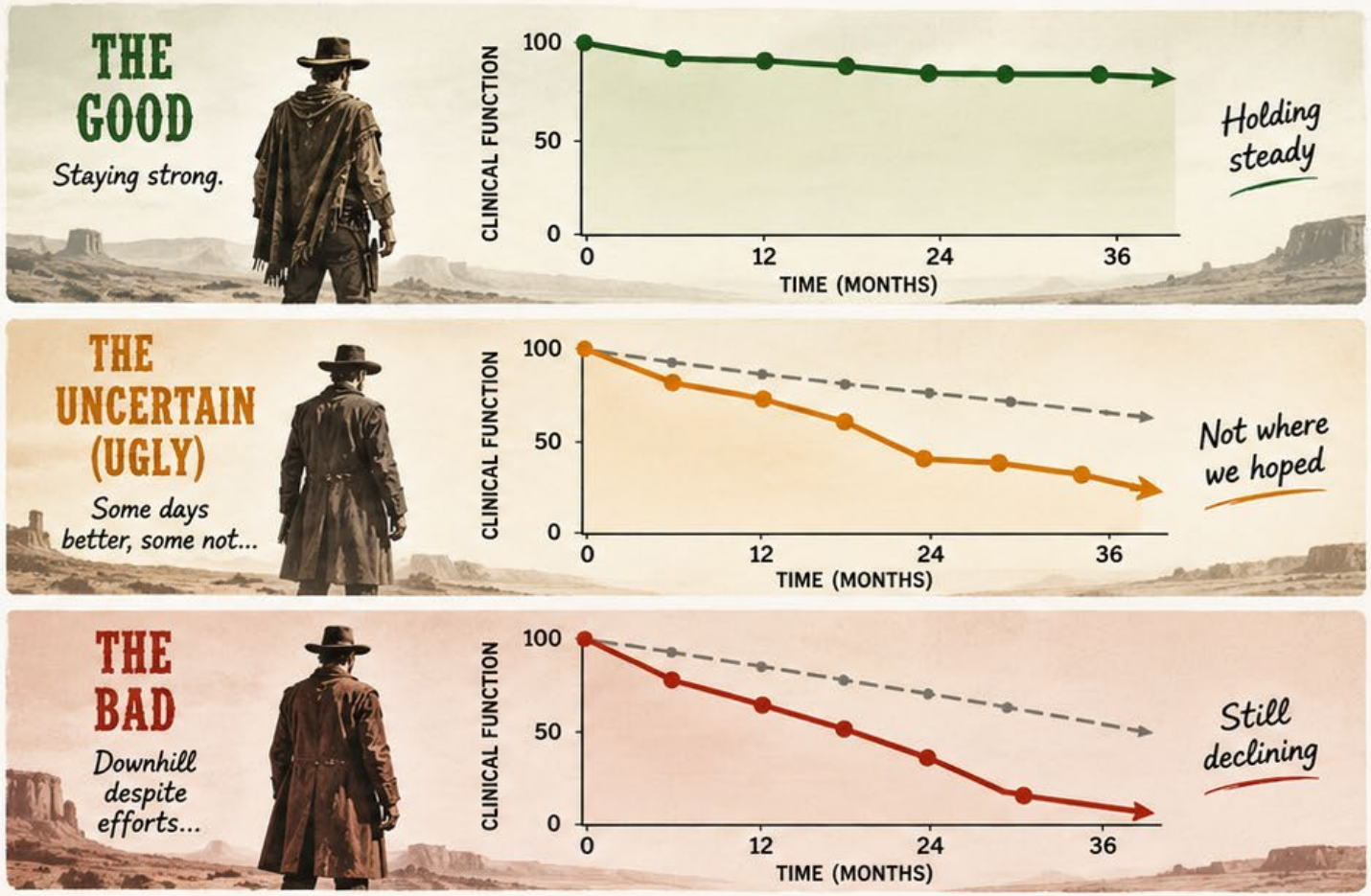
THE BAD

- Continued decline despite measurable biomarker change
- Suggests downstream degeneration may already be entrenched

WHAT DRIVES DIFFERENT TRAJECTORIES

- Baseline burden (amyloid, tau, GFAP/NfL, atrophy)
- Disease stage and phenotype
- Biological modifiers (genetics, vascular disease, comorbidities)

DIFFERENT PATIENTS. DIFFERENT TRAJECTORIES.



GOOD RESPONDER

Low baseline burden → robust biologic response

Baseline Clinical Profile

- Minor baseline impairment
  - Executive phenotype
  - No functional impairment

Amyloid

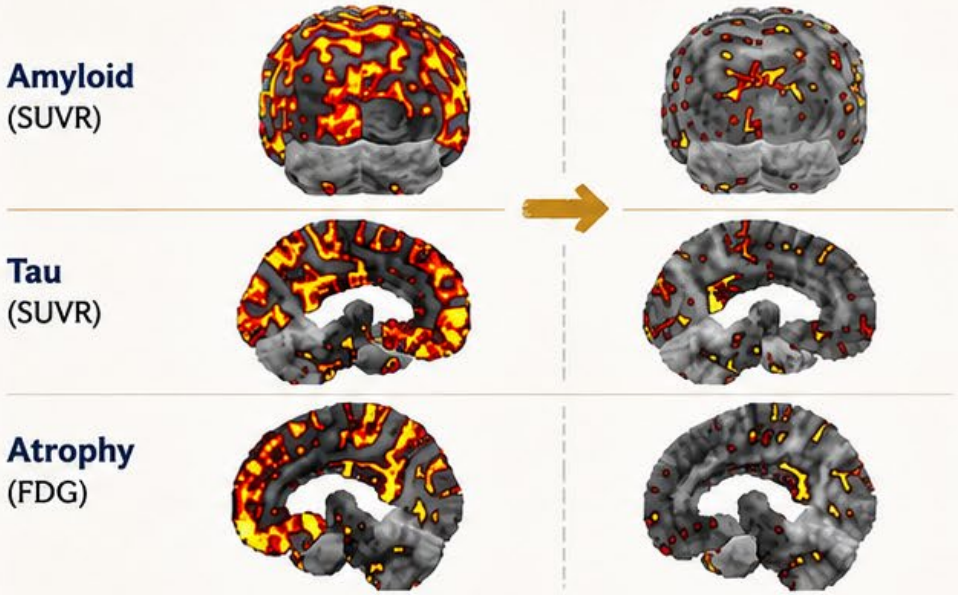
- ↓ Baseline low amyloid (+40 CL)

Tau

- ↓ Baseline pTau (1.0–1.3)

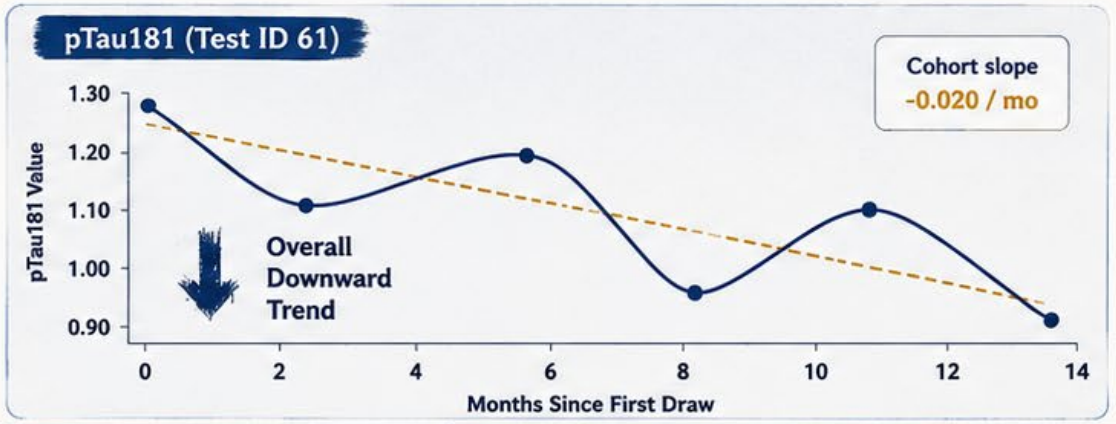
Atrophy Pattern

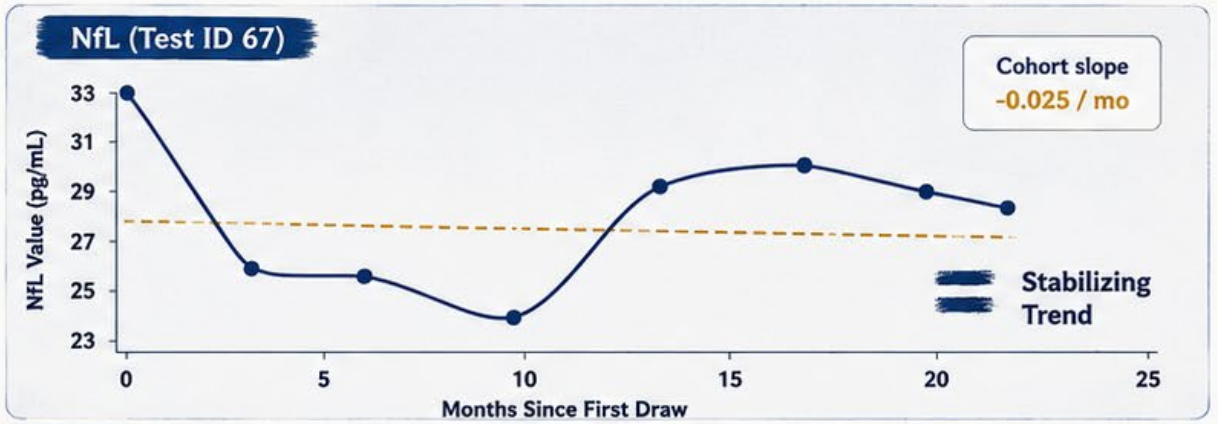
- Mild dorsal cortical volume loss with sparing of subcortical structures
- LOAD-CBS/ADHD presentation



SUMMARY

Low baseline burden across amyloid, tau, and atrophy associates with strong biologic response.





TAKEAWAY: Lower baseline burden, early disease, and strategic network involvement can drive robust biologic response and functional preservation.

Early Disease | Lower Burden | Better Response

BAD RESPONDER

High baseline burden → limited biologic response

Clinical Profile

- Major baseline impairment
  - Later mild dementia functional impairment

Amyloid

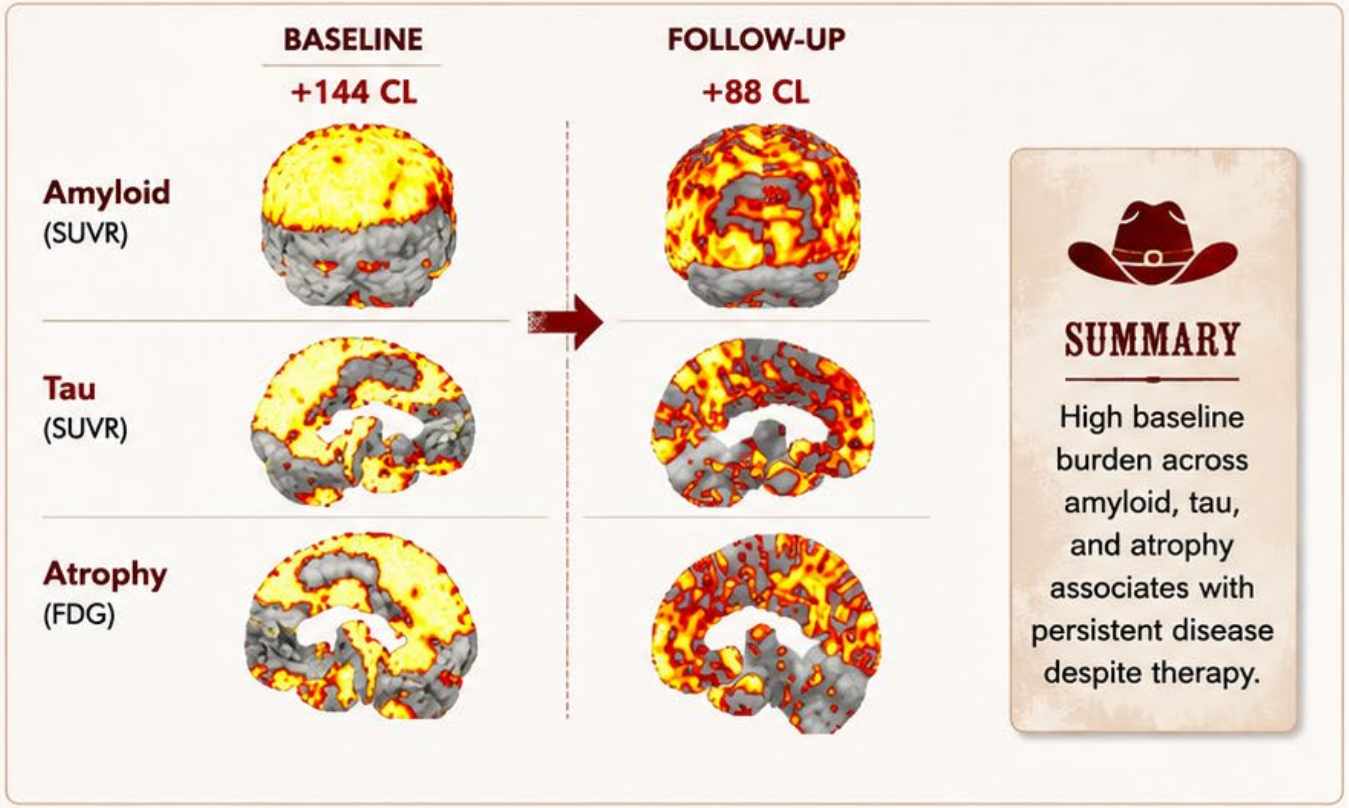
- Severe amyloid >100 CL (PSEN1 mutation)

Tau

- Baseline high >2 pTau181

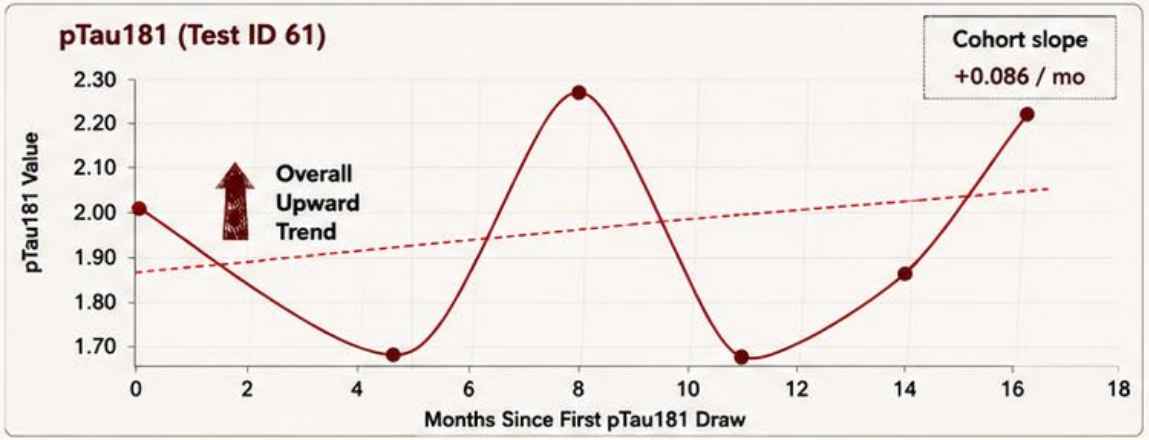
Atrophy Pattern

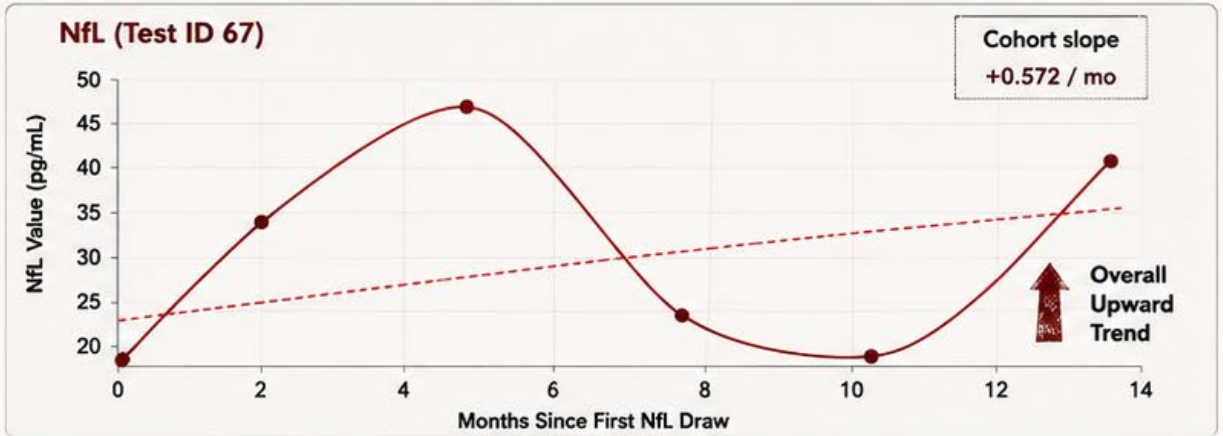
- Moderate generalized atrophy with prominent subcortical atrophy
- Amnestic LOAD or mixed DLB presentation



SUMMARY

High baseline burden across amyloid, tau, and atrophy associates with persistent disease despite therapy.





TAKEAWAY: Severe baseline disease burden, advanced stage, and adverse biology limit response potential and are associated with continued progression.

High Burden | Limited Response | Continued Progression

UNCERTAIN RESPONDER

Intermediate baseline burden → variable biologic response

CLINICAL PROFILE

- Mild to moderate baseline impairment
  - Mild functional impairment

AMYLOID

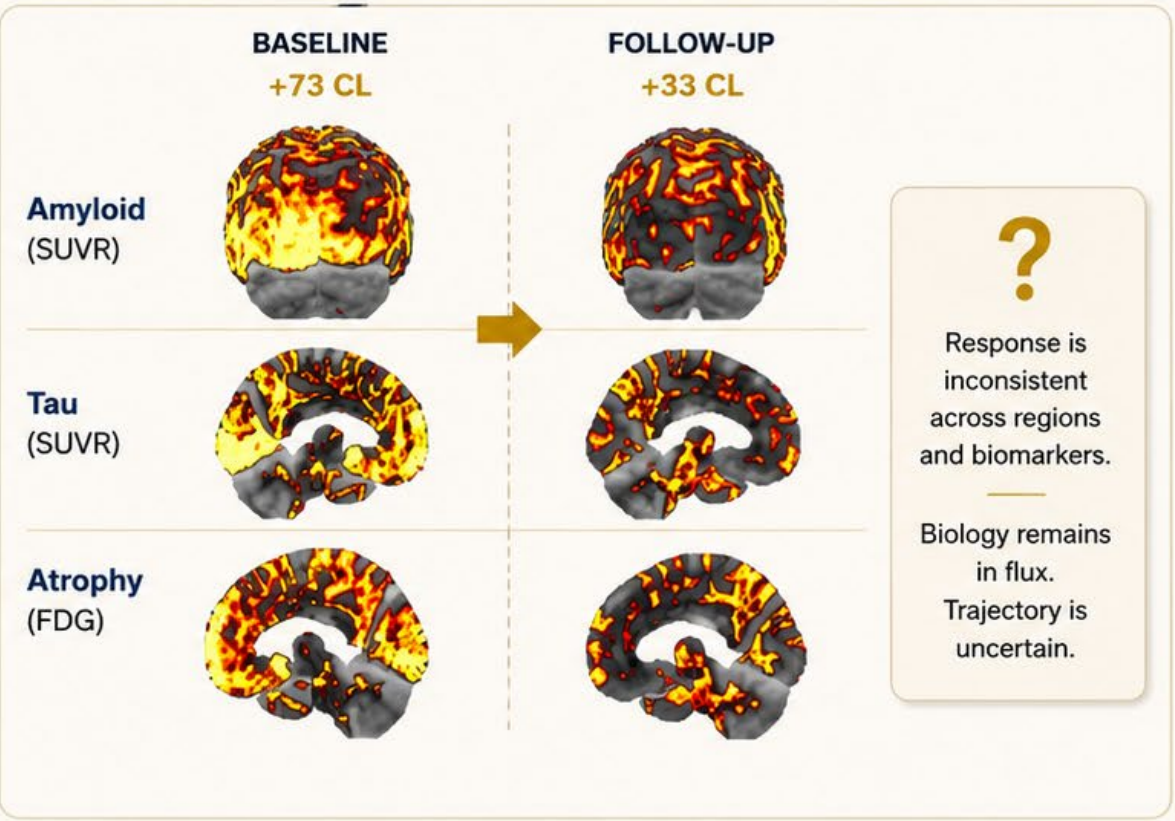
- Moderate baseline amyloid (+73 CL)

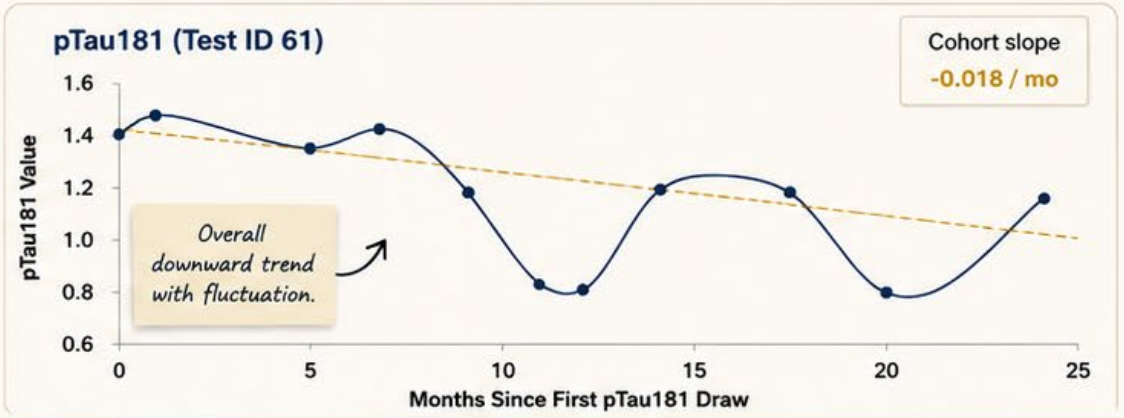
TAU

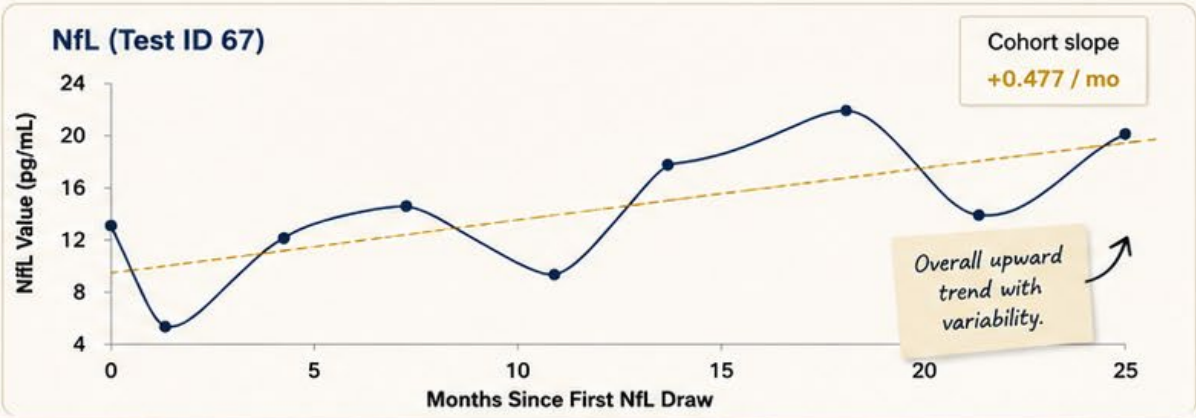
- Baseline 1.3–1.8 pTau181

ATROPHY PATTERN

- Minor generalized atrophy / temporal-parietal cortical volume loss with minor subcortical structures
- LOAD-PCA / lvPPA presentation







TAKEAWAY: Intermediate baseline burden and mixed biomarker response lead to inconsistent trajectories and uncertain outcomes.

Mixed Biology | Uncertain Trajectory | Response Not Uniform

We Measure More—But Understand Less Than We Think

1. CENTILOID ≠ CERTAINTY

- Inter-scan / Inter-rater variability
- *Objective* processing differences
- **Global vs regional mismatch**
  - Ceiling + sensitivity issues at high burden
  - Very high baseline burden → Large reductions → still "positive"

2. DIAGNOSTIC vs. MONITORING vs. PROGNOSTIC BIOMARKERS:

- Imaging vs serum vs clinical trajectory

3. OBJECTIVITY INCREASED— BUT INTERPRETABILITY DID NOT SCALE PROPORTIONALLY.

★ MORE SIGNAL. MORE DATA. MORE QUESTIONS.
OUR JOB: TURN UNCERTAINTY INTO CLARITY. ★

REGIONAL MISMATCH EFFECTS DIAGNOSIS

Global normalization ≠ regional clearance

KEY POINTS

- Global **normalization** can **mask persistent regional pathology**
- Focal signal commonly seen in:
  - Occipital / Posterior cingulate – PCC
  - Lateral temporal cortex – **lvPPA**
  - Dorsal parietal / frontal cortex – CBS

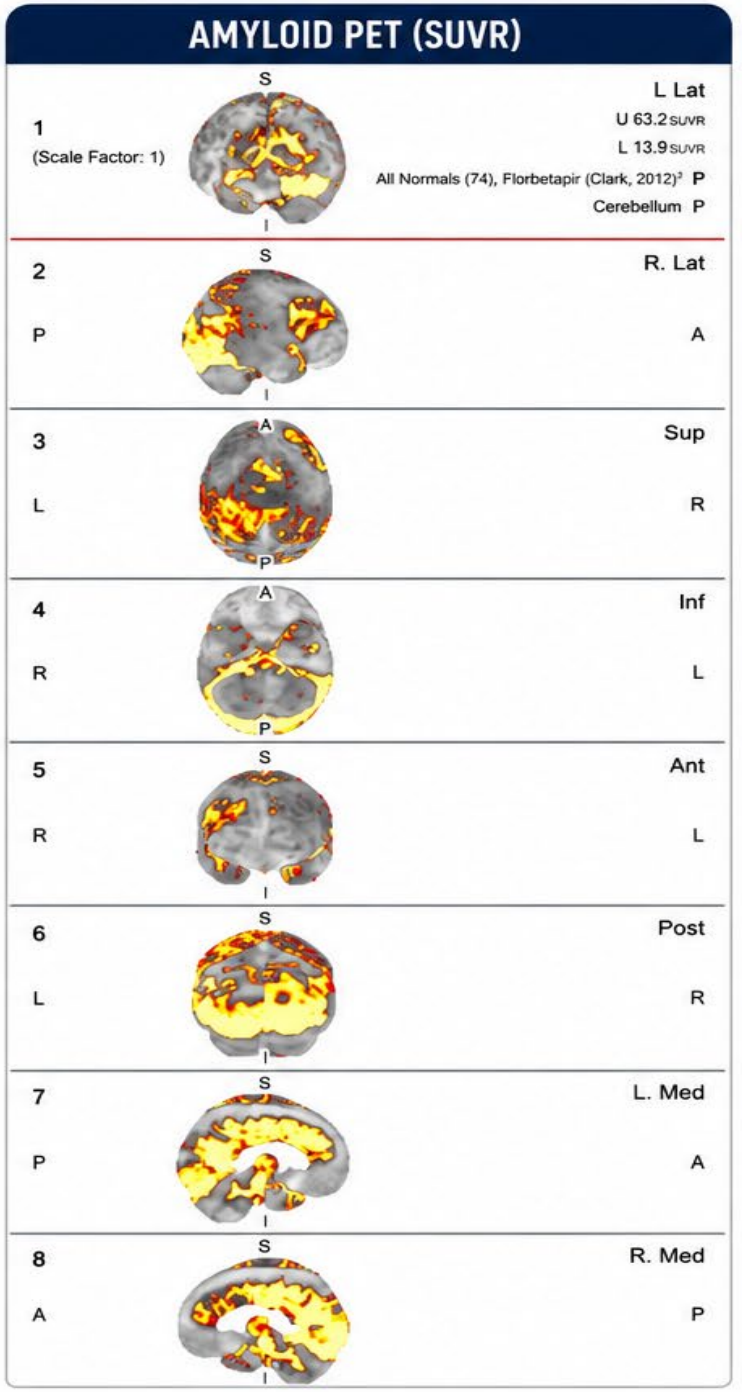
GLOBAL CENTILOID

-17.68

On average, this appears amyloid-negative / low-burden.

But the regional ROI pattern tells a different story.

ROI	Z-SCORE	PATTERN
Posterior Cingulate Gyrus	+13.04	Markedly elevated
Precuneus	+6.91	Markedly elevated
Lateral Temporal Lobe	+0.32	Near normal
Anterior Cingulate Gyrus	-7.57	Low
Inferior Medial Frontal Gyrus	-10.17	Low
Superior Parietal Lobule	-9.88	Low



REGIONAL MISMATCH EFFECTS TREATMENT

Global normalization ≠ regional clearance

KEY MESSAGES

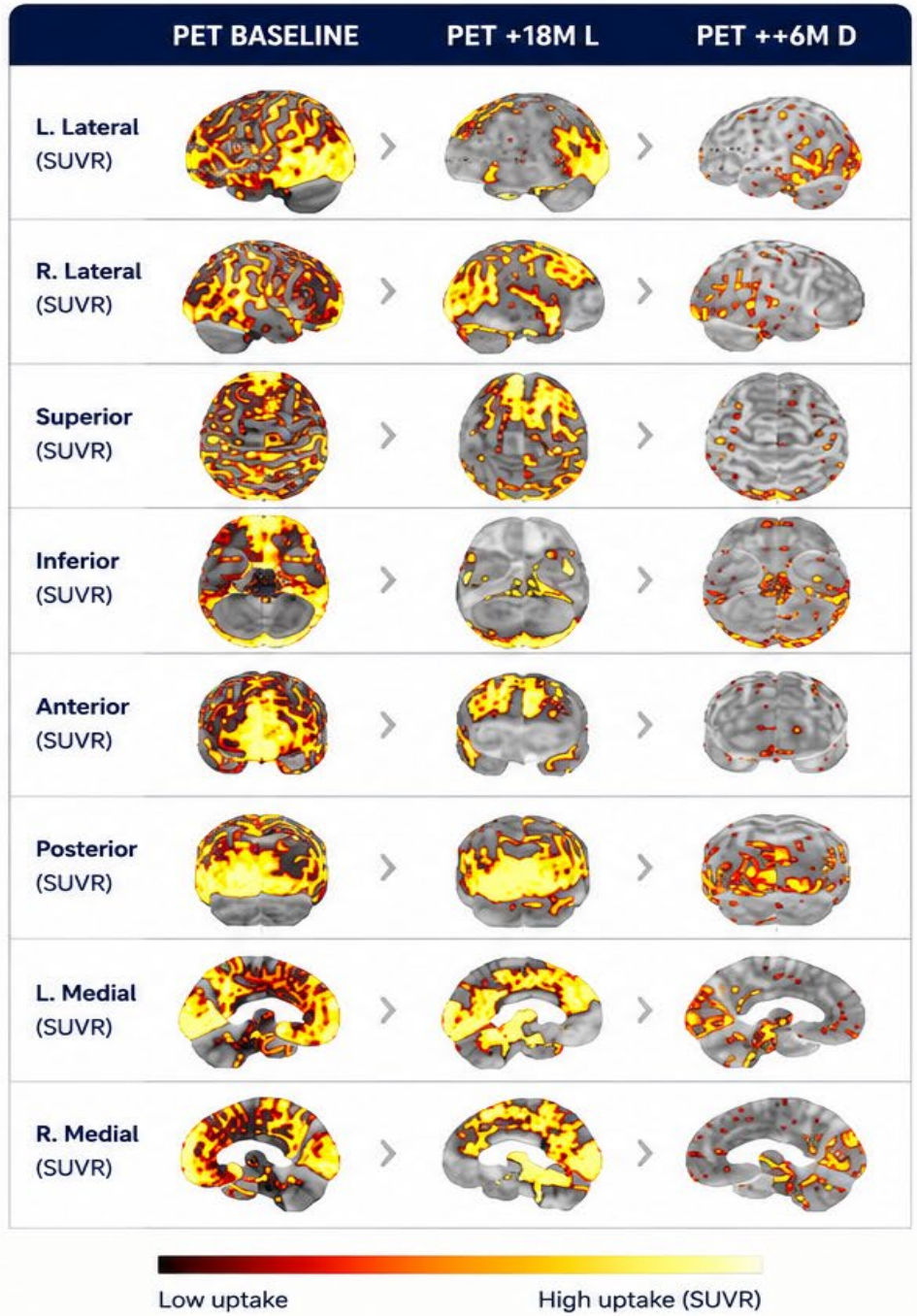
- Global normalization **does not equal regional clearance**
- Persistent signal in:
  - Precuneus
  - Posterior cingulate
  - Lateral temporal cortex
- Serum biomarkers may remain positive

GLOBAL CENTILOID

2024	2025	2026
+64.7	−21.0	−19.3

Global amyloid burden has normalized.
Regional hotspots persist.

REGIONAL ROI Z-SCORES	2025 Z	2026 Z	Δ (2026–2025)	TREND
Anterior Cingulate	-9.35	-4.47	+4.88	↑
Inferior Frontal	-11.82	-4.67	+7.15	↑
Lateral Temporal	-3.57	-3.13	+0.44	→
Posterior Cingulate	+8.52	+1.62	-6.90	↓
Precuneus	+7.63	-0.83	-8.46	↓
Superior Parietal	+0.96	-4.07	-5.03	↓



Diagnostic Biomarker = Monitoring Biomarkers?

The biology is dynamic. Life happens.

1 DISEASE IS:

- Nonlinear
- Vulnerable to disruption

BIOMARKERS ARE SIGNALS, NOT ANSWERS. | INTEGRATE BIOLOGY. EXPECT VARIABILITY. ACT WITH CONTEXT.

Diagnostic Biomarkers ≠ Prognostic Biomarkers

Anti-amyloid therapy has changed the central clinical question.

We are no longer simply asking:

"Does this patient have Alzheimer's disease?"

We are increasingly being forced to ask:

"What happens biologically after treatment?"

Fast Reaccumulator of Amyloid

In just 6 months off AAT, they reaccumulated ~10 CL

ON AAT (Baseline)

Centiloid Value
-21.53
Global SUVR
0.88
(±1.14)

6 MONTHS OFF AAT

~10 CL
Reaccumulated in 6 months

OFF AAT (6 Months)

Centiloid Value
-12.65
Global SUVR
0.93
(±1.14)

Regional SUVR Changes

Increase in amyloid across key regions

ROI	ON AAT (Baseline)	OFF AAT (6 Months)	CHANGE
Anterior Cingulate Gyrus	0.87	1.08	+0.21
Inferior Medial Frontal Gyrus	0.85	0.97	+0.12
Lateral Temporal Lobe	1.01	0.78	+0.23
Posterior Cingulate Gyrus	0.83	0.78	+0.05
Precuneus	0.89	1.02	+0.13
Superior Parietal Lobule	0.86	0.98	+0.12

Substantial amyloid reaccumulation in just 6 months off AAT

~10 Centiloid increase across the brain

When Do We Stop? It's Not Simple

Stopping anti-amyloid therapy is not just a clinical decision—
it is a deeply personal and value-based decision.

WHEN WE CONSIDER STOPPING

Clear clinical checkpoints help guide the conversation.

1. **FAST 5 OR MODERATE STAGE**
   Disease progression despite treatment or limited meaningful benefit.
2. **LOSS OF BASIC ADLs**
   Clearly due to cognition, with ongoing functional decline.
3. **DISPROPORTIONATE BURDEN**
   Treatment burden, safety risks, or diminishing return.
4. **PATIENT AND FAMILY GOALS**
   Shift toward comfort, quality, and meaning over disease modification.

WHAT WE MUST STILL WEIGH

Important benefits may remain— even in later stages.

- **STABILITY MATTERS**
  Treatment may be slowing decline, even if changes are subtle.
- **HUMAN CONNECTION**
  Quality time, engagement, and moments that still matter.
- **SENSE OF PURPOSE**
  Participation in activities, routines, and relationships.
- **PATIENT AND FAMILY PREFERENCE**
  Values, wishes, and acceptable trade-offs are unique to each person.

OUR APPROACH

Shared decision-making.
Reassess regularly. Respect what matters most.

WHEN WE TRANSITION

Focus shifts to comfort, dignity, and quality of life.

THIS IS NOT A STOP SIGN. IT'S A GUIDEPOST. | WE WALK THIS PATH TOGETHER.

WHAT ACTUALLY CHANGED

THE FRONTIER JUST OPENED.

THE GOOD

We can finally see the biology in motion.

- Amyloid can be reduced
- Tau and injury markers can shift
- Earlier intervention appears to matter
- Some patients remain stable longer than expected

THE BAD

Treatment made the disease harder to ignore.

- Monitoring became continuous
- Decisions became heavier and more complex
- Biomarkers created new ambiguity
- The burden of care became visible in real time

THE UNCERTAIN

Biology and human trajectory still do not fully align.

- Some patients dramatically improve
- Some partially respond
- Some continue to decline despite measurable change
- We still cannot fully predict who follows which path

BUT THE FRONTIER DID NOT CLOSE.

Anti-amyloid therapy did not "solve" Alzheimer's. It opened a new territory to explore.

WE ARE LEARNING:

- how to intervene earlier
- how to stratify risk better
- how to personalize therapy more intelligently
- and how much remains undiscovered

THE UNCERTAINTY REMAINS— BUT NOW WE CAN MOVE FORWARD WITH PURPOSE.

The science is advancing. The path is becoming clearer. The work continues.

Ochsner Neurocognitive Program

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