15ème CONGRÈS de la Société de Gérontologie de Bordeaux et du Sud-Ouest

“ ÇA CHAUFFE EN GÉRIATRIE !

9 et 10 oct. 2025 | LE CONNECTEUR BIARRITZ

SGBSO SOCIÉTÉ DE GÉRONTOLOGIE DE BORDEAUX ET DU SUD-OUEST

L’immunothérapie anti-amyloïde : des principaux résultats jusqu’à l’avis défavorable de la HAS

Julien Delrieu - IHU HealthAge, CMRR *Toulouse, France*

UNIVERSITÉ TOULOUSE III PAUL SABATIER

CERPOP

IHU HealthAge GEROSCIENCE & PREVENTION

CHU TOULOUSE

Liens d’intérêt

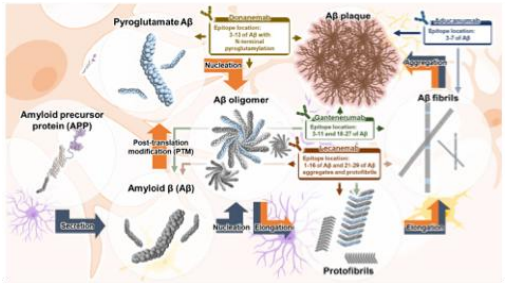
- Consultant : Roche (2020-2022), Eisai (2023-2025), Regenlife (2021-2023), Vaincre Alzheimer (2023-2025), Lilly (2024-2025) NovoNordisk (2024), France Alzheimer (2024-2025)

- Conférence : Biogen (2021), Roche (ateliers, 2021-2022), Eisai (2024), NovoNordisk (2024)

- PI des études : LIGHT4LIFE (NCT05926011, Regenlife), LOCUS-TAU (Vaincre Alzheimer), A3D (PHRC, GIRCI SOHO), TIRAD (IHU HeathAge)

Les traitements de la MA à « visée cognitive »

1993	2000–2010	2010–2015	2015–2020	2020–2023
FDA approval for cholinesterase inhibitors	Anti-Aβ mAb RCTs	Anti-Aβ mAb RCTs in early AD	Anti-Aβ mAb RCTs in early biomarker-confirmed AD	3 phase III anti-Aβ mAb RCTs meeting (at least) the primary endpoint
1990	2000	2010	2015	2020	2023



GAPS

- Questionable clinical meaningfulness
- Risk of ARIA and infusion-related reactions
- High costs
- Complexity of administration and monitoring procedures
- Limited knowledge in certain populations

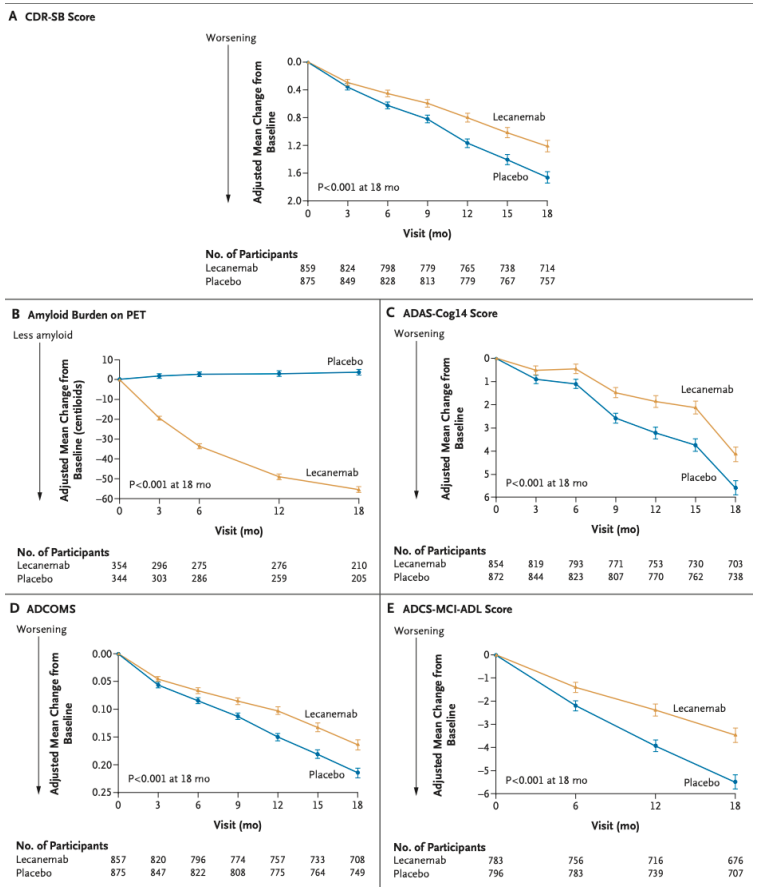
PERSPECTIVES

- New generation anti-Aβ mAbs (e.g., brain shuttle)
- Subcutaneous and oral anti-Aβ drug formulations
- New pharmaceutical targets in amyloid cascade (e.g., oligomers)
- New non-amyloid pharmaceutical targets (e.g., geroprotectors, anti-MTBR-tau mAbs)
- Combined therapies – Multi-target therapies
  Precision medicine therapies

Angioni D, Delrieu J, Coley N, Ousset PJ, Shi J, Vellas B. Drugs for Alzheimer's disease: Where are we coming from? Where are we going? Sci Bull (Beijing). 2024 May 30;69(10):1369-1374.
Kim BH, Kim S, Nam Y, Park YH, Shin SM, Moon M. Second-generation anti-amyloid monoclonal antibodies for Alzheimer's disease: current landscape and future perspectives. Transl Neurodegener. 2025 Jan 27;14(1):6.

Lécanémab : essai clinique de Phase III

Résultats de l'étude CLARITY AD (n=1795, 18 mois)



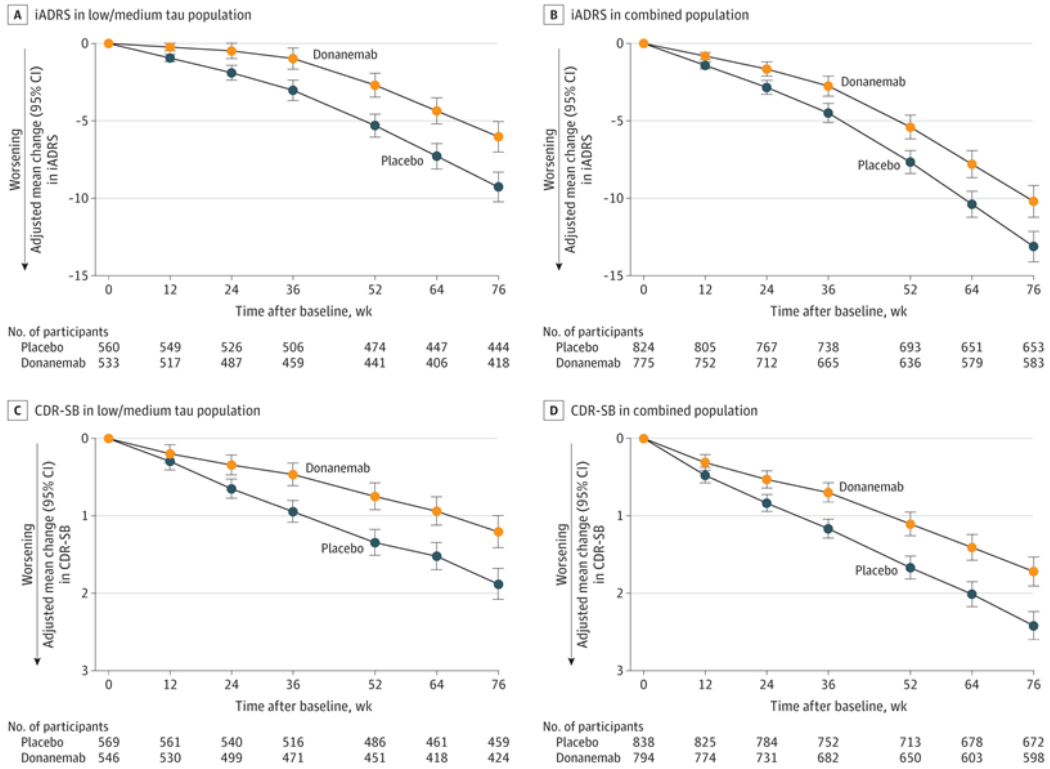
Dans la MA prodromale à légère A+

- **Efficacité** : ralentissement de 27% du déclin cognitif à 18 mois (CDR-SB, -0,45), effet cohérent sur tous les critères de jugement secondaires (ADAS-cog, ADCS-MCI-ADL,ADCOMS, charge amyloïde)
- **Administration** : IV de manière bimensuelle
- **Effets indésirables** : ARIA (ARIA-E 12,6%, ARIA-H 17,3%), réaction liées à la perfusion (26,4%)

Van Dyck CH, Swanson CJ, Aisen P, Bateman RJ, Chen C, Gee M, Kanekiyo M, Li D, Reyderman L, Cohen S, Froelich L, Katayama S, Sabbagh M, Vellas B, Watson D, Dhadda S, Irizarry M, Kramer LD, Iwatsubo T. Lecanemab in Early Alzheimer's Disease. N Engl J Med. 2023 Jan 5;388(1):9-21.

Donanémab : essai clinique de Phase III

Résultats de l'étude TRAILBLAZER II (n=1736, 18 mois)



Dans la MA prodromale à légère A+

- **Efficacité** : ralentissement de 22,3-35,1% du déclin cognitif à 18 mois (iADRS -3,25, plus important pour charge Tau faible/intermédiaire à baseline)
- **Administration** : IV de manière mensuelle
- **Effets indésirables** : ARIA (ARIA-E 24%, ARIA-H 19,7%) et réactions liées à la perfusion (8,7%)

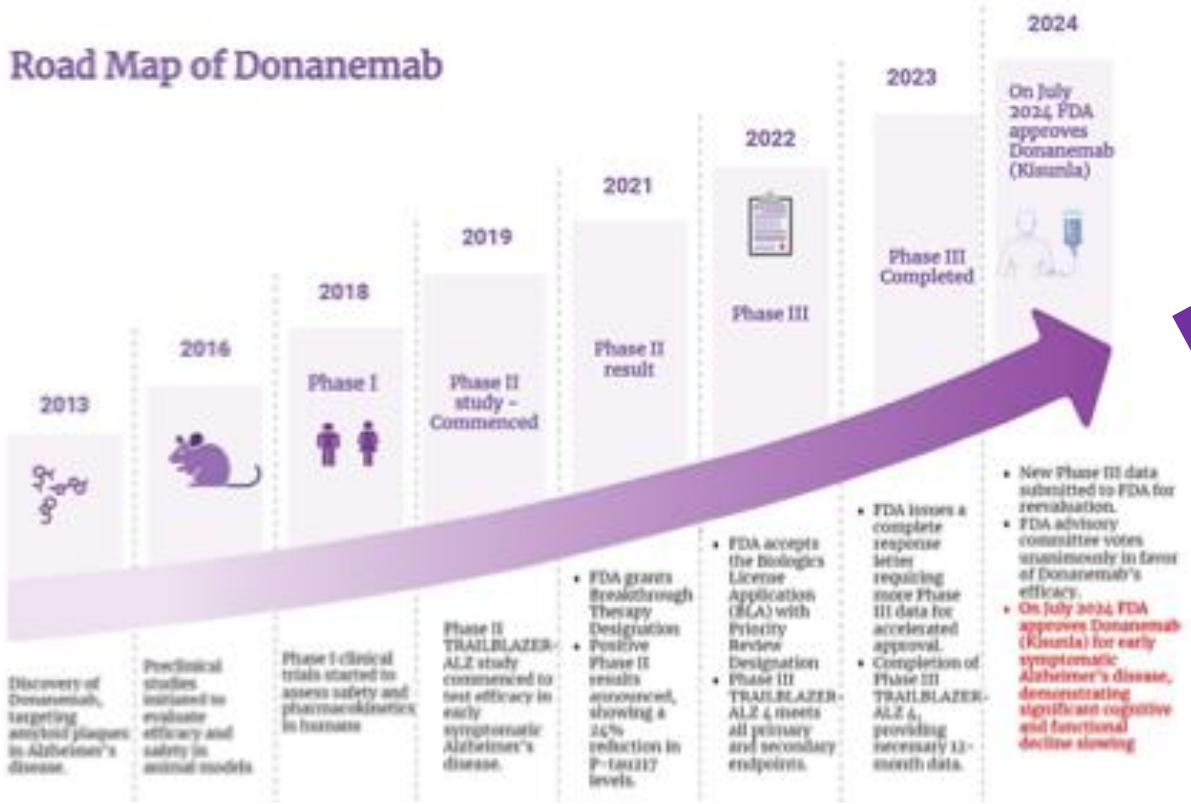
Sims JR, Zimmer JA, Evans CD, Lu M, Ardayfio P, Sparks J, Wessels AM, Shcherbinin S, Wang H, Monkul Nery ES, Collins EC, Solomon P, Salloway S, Apostolova LG, Hansson O, Ritchie C, Brooks DA, Mintun M, Skovronsky DM; TRAILBLAZER-ALZ 2 Investigators. Donanemab in Early Symptomatic Alzheimer Disease: The TRAILBLAZER-ALZ 2 Randomized Clinical Trial. JAMA. 2023 Aug 8;330(6):512-527.

Les recommandations nationales sur l'utilisation du leqembi qui précèdent l'AMM européenne

Pays	Indication clinique	Biomarqueurs	Contre-indications	IRM	Arrêt du traitement
France (Fédération des Centres Mémoire)	Trouble cognitif mineur (MCI) ou trouble cognitif majeur de sévérité légère dû à la MA **Phénotype commun de MA : syndrome amnésique hippocampique, syndrome de Benson, APP logopénique**	**Confirmation A+T+** **Biomarqueurs sanguins (ptau217) avec double-seuil si disponible** Biomarqueurs du LCR si biomarqueurs sanguins non disponibles ou en zone grise TEP amyloïde si CI à la PL ou biomarqueurs du LCR discordants	**Anticoagulants** Coagulopathie **APOE4 homozygotes** **Angiopathie amyloïde** Contre-indication à la réalisation du monitoring IRM Contre-indications IRM (>4 micro saignements, sidérose superficielle, HIC>10 mm, leucopathie Fazekas >2, angiopathie amyloïde, infarctus lacunaire multiple, ARIA-E)	IRM initiale dans les **6 mois** qui précèdent l'initiation du traitement **IRM avant la 3ème**, 5ème, 7ème et 14ème perfusion **Avant la 27ème pour les patients porteurs APOE4 et avec ARIA**	Macrohémorragie ≥ + 10 microsaignements/début du traitement > 1 site de sidérose superficielle > 2 épisodes d'ARIA Symptômes sévères d'ARIA Introduction d'anticoagulant Stades modéré/sévère de la MA
Etats-unis (Alzheimer's Disease and Related Disorders Therapeutics Work Group)	Trouble cognitif léger (MCI) ou démence légère due à la MA MMSE 22-30	Confirmation d'une amyloïdopathie (TEP amyloïde et/ou biomarqueurs du LCR)	Anticoagulants Coagulopathie ABRA, AAC-i Contre-indications IRM (>4 micro saignements, sidérose superficielle, HIC, leucopathie Fazekas >2, angiopathie amyloïde, >2 lacunes, ARIA-E)	IRM dans l'année précédant l'initiation du traitement IRM avant la 5ème, 7ème et 14ème perfusion Avant la 26ème pour les patients porteurs APOE4 et avec ARIA	Macrohémorragie ≥ + 10 microsaignements/début du traitement > 1 site de sidérose superficielle > 2 épisodes d'ARIA Symptômes sévères d'ARIA Introduction d'anticoagulant
Corée (Korean Dementia Association)	Trouble cognitif léger (MCI) ou démence légère due à la MA CDR 0,5-1	Confirmation d'une amyloïdopathie (TEP amyloïde et/ou biomarqueurs du LCR)	Anticoagulants Coagulopathie ABRA, AAC-i Contre-indications IRM (>4 micro saignements, sidérose superficielle, HIC, leucopathie Fazekas >2, angiopathie amyloïde, >2 lacunes, ARIA-E)	IRM dans l'année précédant l'initiation du traitement IRM avant la 5ème, 7ème et 14ème perfusion Avant la 26ème pour les patients porteurs APOE4 et avec ARIA	Stades modéré/sévère de la MA

Cummings J, Apostolova L, Rabinovici GD, Atri A, Aisen P, Greenberg S, et al. Lecanemab: Appropriate Use Recommendations. J Prev Alzheimers Dis. 2023;10(3):362–77.
Villain N, Planche V, Lilamand M, Cordonnier C, Soto-Martin M, Mollion H, et al. Lecanemab for early Alzheimer's disease: Appropriate use recommendations from the French federation of memory clinics. J Prev Alzheimers Dis. 2025 Apr;12(4):100094.
Jeon SY, Wang SM, Roh HW, Kim KY, Chang YY, Kim E, et al. Practical Guide of the Korean Association for Geriatric Psychiatry to Anti-Amyloid Monoclonal Antibody Therapy for Alzheimer's Disease: Focused on Lecanemab. J Korean Med Sci. 2025 July 21;40(28):e215.

Avis défavorable puis favorable du CHMP pour le Kisunla



- Refus du CHMP le 28 mars 2025
- Après ré examen, avis favorable du CHMP dans une indication similaire au leqembi+AMM UE en septembre

Pays ayant approuvé le donanemab (Kisunla)

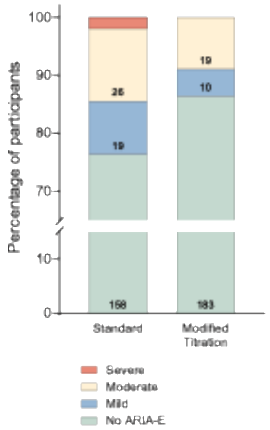
Jayaprakash N, Elumalai K. Translational Medicine in Alzheimer's Disease: The Journey of Donanemab From Discovery to Clinical Application. Chronic Dis Transl Med. 2024 Dec 16;11(2):105-116.

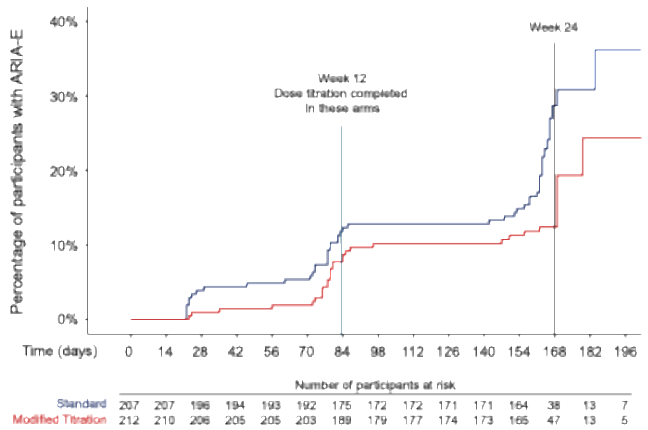
Titration modifiée du Donanémab

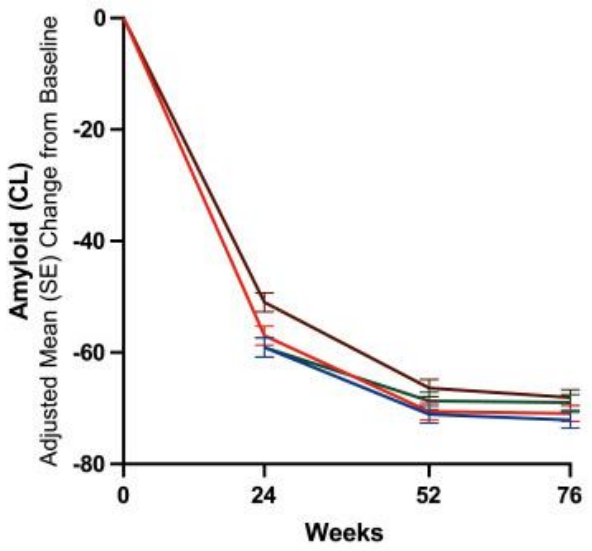
Effet sur les ARIA et la charge amyloïde

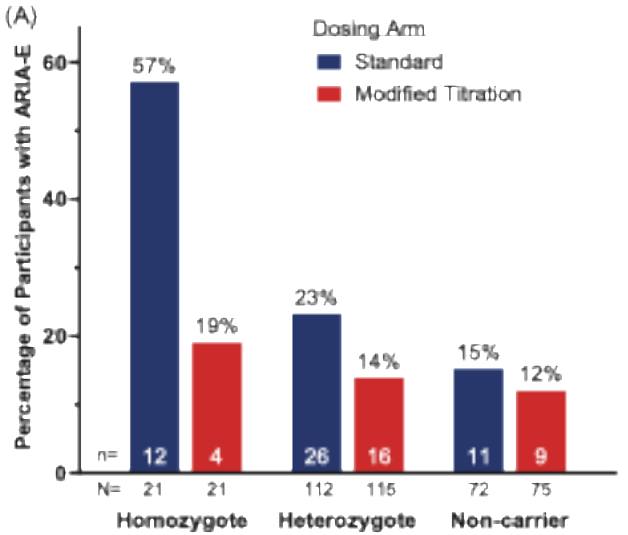
1:1:1:1 Randomization stratified by APOE and by baseline amyloid — Primary Outcome

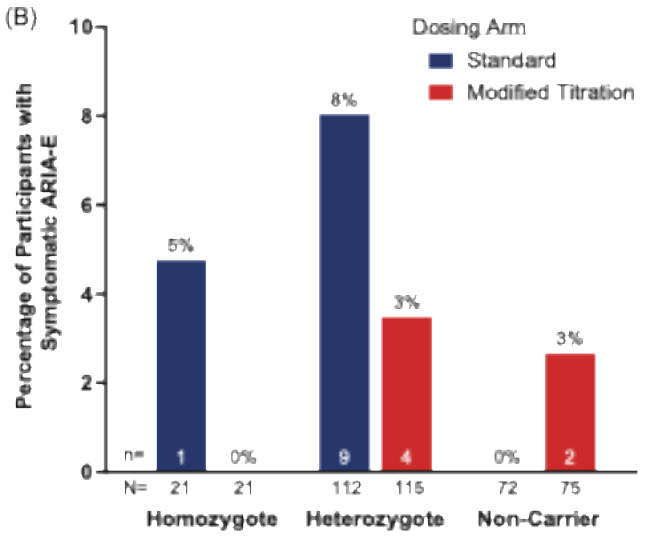
Visit number	1	2	3	4	5	6	7	8	9	10	11	12
Study week	Screening	0	2	4	6	8	10	12	14	16	20	24
Standard		700	PBO	700	PBO	700	PBO	1400	PBO	1400	1400	1400
Modified titration		350	PBO	700	PBO	1050	PBO	1400	PBO	1400	1400	1400
Dose skipping		700	PBO	PBO	PBO	1400	PBO	1400	PBO	1400	1400	1400
Cmax		350	350	350	350	350	350	700	700	1400	1400	1400





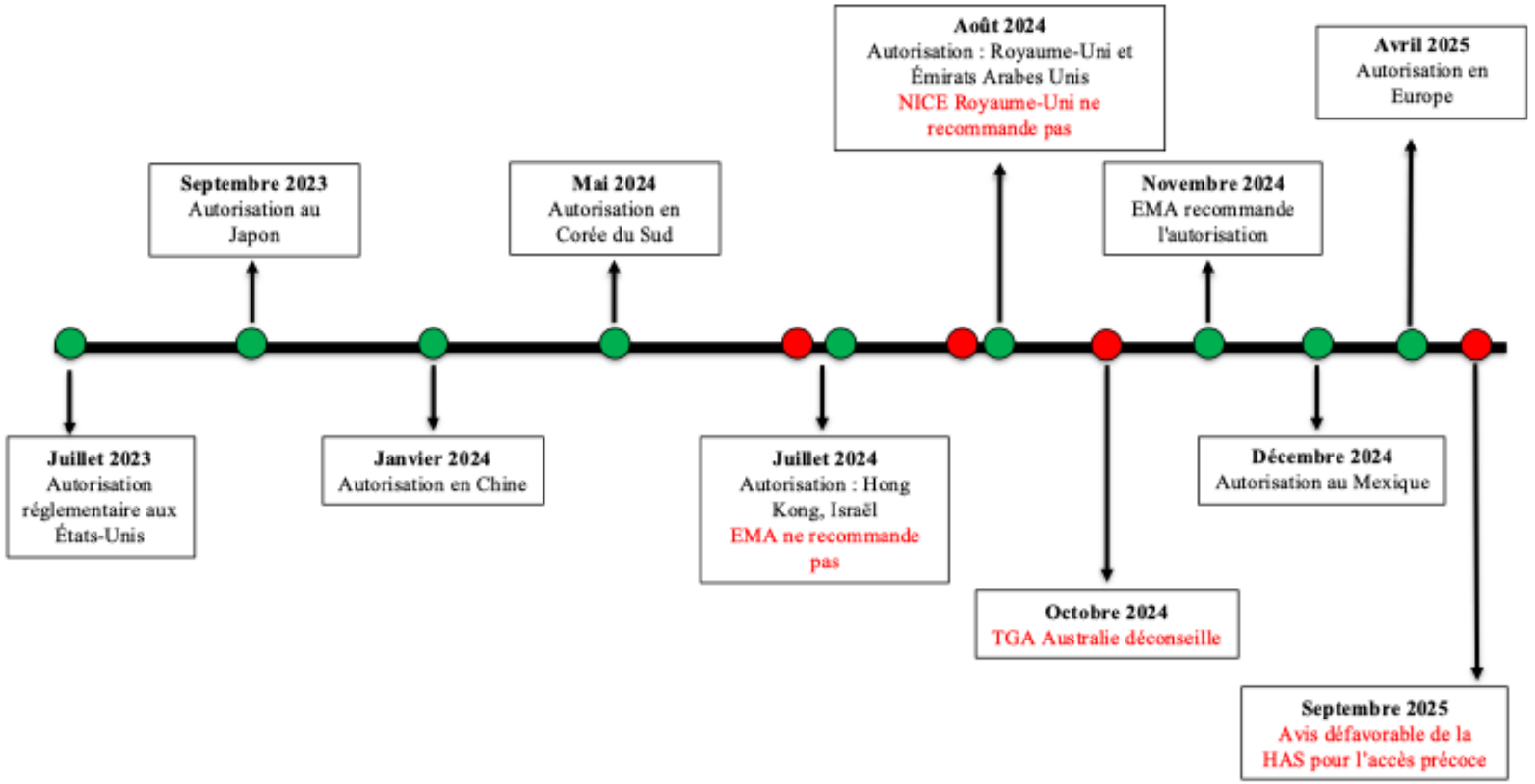


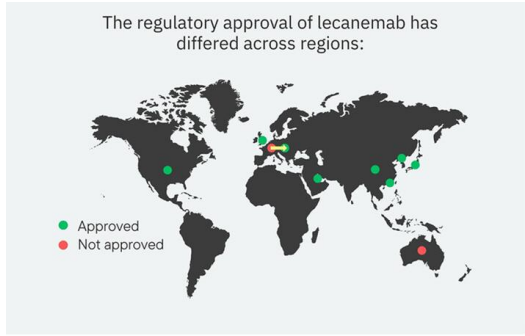




Wang H, Nery ESM, Ardayfio P, Khanna R, Svaldi DO, Shcherbinin S, Xu W, Andersen SW, Hauck PM, Brooks DA, Collins EC, Salloway S, Mintun MA, Sims JR. The effect of modified donanemab titration on amyloid-related imaging abnormalities with edema/effusions and amyloid reduction: 18-month results from TRAILBLAZER-ALZ 6. J Prev Alzheimers Dis. 2025 Jul 5:100266.

Autorisation du Leqembi en Europe





Bobbins A, Davies M, Lynn E, Roy D, Yeomans A, Shakir SAW. Safety and effectiveness of the anti-amyloid monoclonal antibody (mAb) drug lecanemab for early Alzheimer's disease: The pharmacovigilance perspective. Br J Clin Pharmacol. 2025 May;91(5):1352-1360.

Pourquoi un avis défavorable pour le Leqembi ?

La maladie d’Alzheimer est une maladie grave et invalidante sans traitement approprié MAIS le leqembi peut être différé et n’est pas susceptible d’être innovant…

Critères d’accès précoce « non remplis »		Avis de la Haute Autorité de Santé	Avis d’un clinicien impliqué dans la PEC des patients
PEUT ETRE DIFFERE	**Effet clinique**	Non cliniquement pertinent	Effet clinique à 18 mois, effet clinique cumulatif probable
NON SUSCEPTIBLE D’ETRE INNOVANT	**Effets indésirables**	Profil de tolérance préoccupante nécessitant une adaptation du parcours de soins	Etude PASS et registre en vie réelle Exclusion des patients sous anticoagulants et APOE4 homozygotes Environ 1% EIG Recommandations FCM
	Génotypage APOE	Faisabilité et problème éthique	Fait en pratique de manière non systématique Consentement génétique (FCM) Pas de conseil génétique pour les descendants Décision partagée
	Parcours de soins	Préoccupante nécessitant une modification du parcours de soins	Nombre restreint de patients la première année, environ 1500 répartis sur plus de 30 CMRR, 8% de la population Mémoire
	Association entre la diminution de charge amyloïde et l’effet clinique	Pas de relation claire	Méta-analyse récente
	Effet sur la charge amyloïde	Biais de sélection potentiel (40%)	Effet de classe connu déjà mis en évidence avec le bapineuzumab en 2010 (n=28, 78 semaines)
	Atrophie	Atrophie induite par ARIA potentiellement péjorative sur le long terme	Inflammation ? Pseudo-atrophie ?
	Qualité de vie	Analyse exploratoire	Effet sur qualité de vie et fardeau de l’aidant

Pertinence clinique de -0,5 point CDR-SB ?

Est-il vraiment pertinent d’évaluer le caractère cliniquement pertinent d’un traitement modificateur de la maladie à 18 mois?

	Impairment				
	None 0	Questionable 0.5	Mild 1	Moderate 2	Severe 3
Memory	No memory loss or slight inconsistent forgetfulness	Consistent slight forgetfulness; partial recollection of events; "benign" forgetfulness	Moderate memory loss; more marked for recent events; defect interferes with everyday activities	Severe memory loss; only highly learned material retained; new material rapidly lost	Severe memory loss; only fragments remain
Orientation	Fully oriented	Fully oriented except for slight difficulty with time relationships	Moderate difficulty with time relationships; oriented for place at examination; may have geographic disorientation elsewhere	Severe difficulty with time relationships; usually disoriented to time, often to place	Oriented to person only
Judgment & Problem Solving	Solves everyday problems & handles business & financial affairs well; judgment good in relation to past performance	Slight impairment in solving problems, similarities, and differences	Moderate difficulty in handling problems, similarities, and differences; social judgment usually maintained	Severely impaired in handling problems, similarities, and differences; social judgment usually impaired	Unable to make judgments or solve problems
Community Affairs	Independent function at usual level in job, shopping, volunteer and social groups	Slight impairment in these activities	Unable to function independently at these activities although may still be engaged in some; appears normal at first glance	No possibility of independent function outside home Appears well enough to be taken to functions outside a family home	Appears too ill to be taken to functions outside a family home
Home and Hobbies	Life at home, hobbies, and intellectual interests well maintained	Life at home, hobbies, and intellectual interests slightly impaired	Mild but definite impairment of function at home; more difficult tasks abandoned; more complicated hobbies and interests abandoned	Only simple tasks preserved; very restricted interests, poorly maintained	No significant ability to do things in home
Personal Care	Fully capable of self-care		Needs prompting	Requires assistance in dressing, hygiene, keeping of personal belongings	Requires much help with personal care; frequent incontinence

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Patients dans le groupe actif
A 18 mois : CDR-SB 4

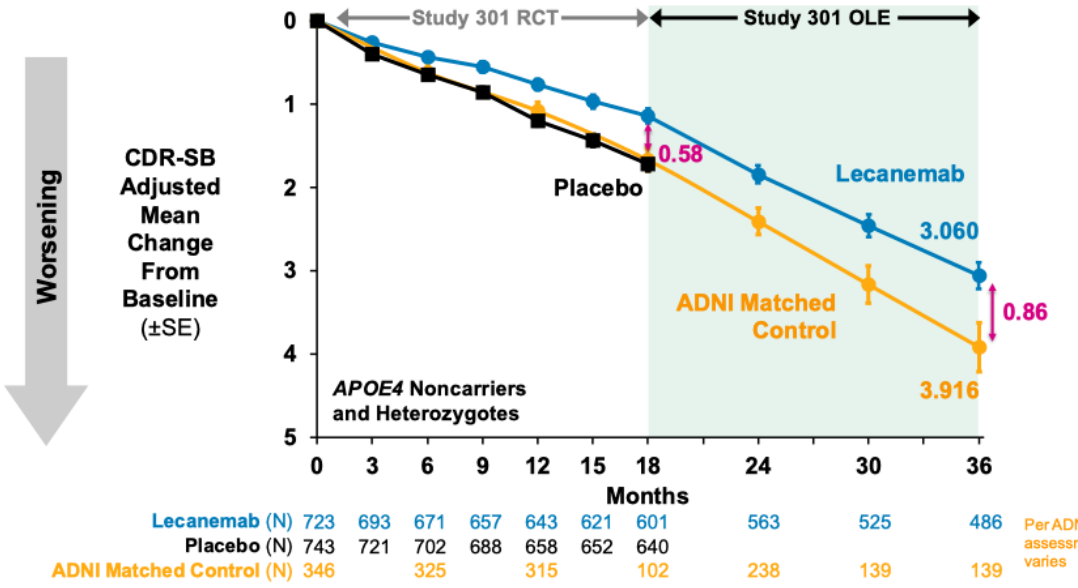
Patients dans le groupe placebo
A 18 mois : CDR-SB 4,5

Déclin léger dans les activités domestiques, les activités de loisir abandonnés, une perte d’intérêt…

Clarity AD OLE : les résultats CDR-SB à 36 et 48 mois

L’immunothérapie peut-elle vraiment être retardée ?

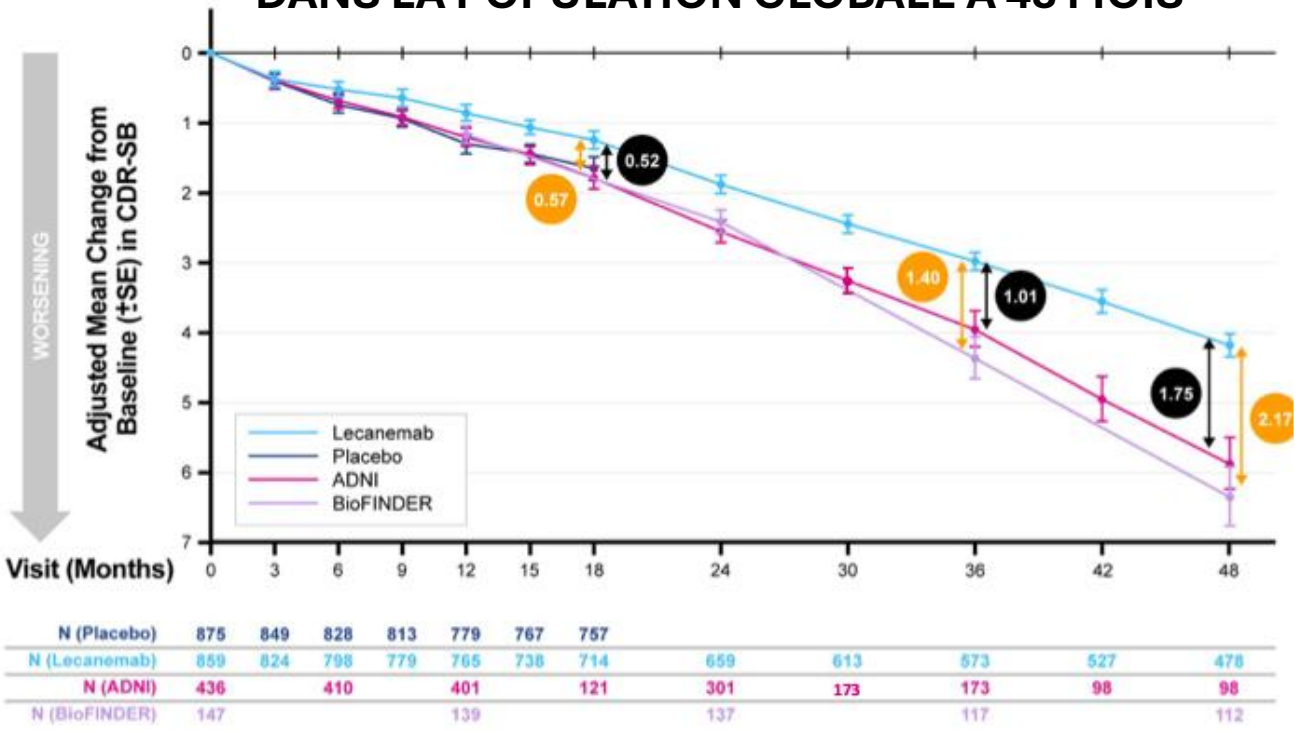
DANS LA POPULATION EUROPENNE A 36 MOIS



Lecanemab (N)	723	693	671	657	643	621	601	563	525	486
Placebo (N)	743	721	702	688	658	652	640			
ADNI Matched Control (N)	346		325		315		102	238	139	139

Per ADNI protocol, assessment timing varies

DANS LA POPULATION GLOBALE A 48 MOIS



N (Placebo)	875	849	828	813	779	767	757					
N (Lecanemab)	859	824	798	779	765	738	714	659	613	573	527	478
N (ADNI)	436		410		401		121	301	173	173	98	98
N (BioFINDER)	147				139			137		117		112

Van Dick C. AAIC, Toronto, Canada, July 2025.

Note: OLE includes those participants on subcutaneous and intravenous formulations. BioFINDER data are from BioFINDER 1.

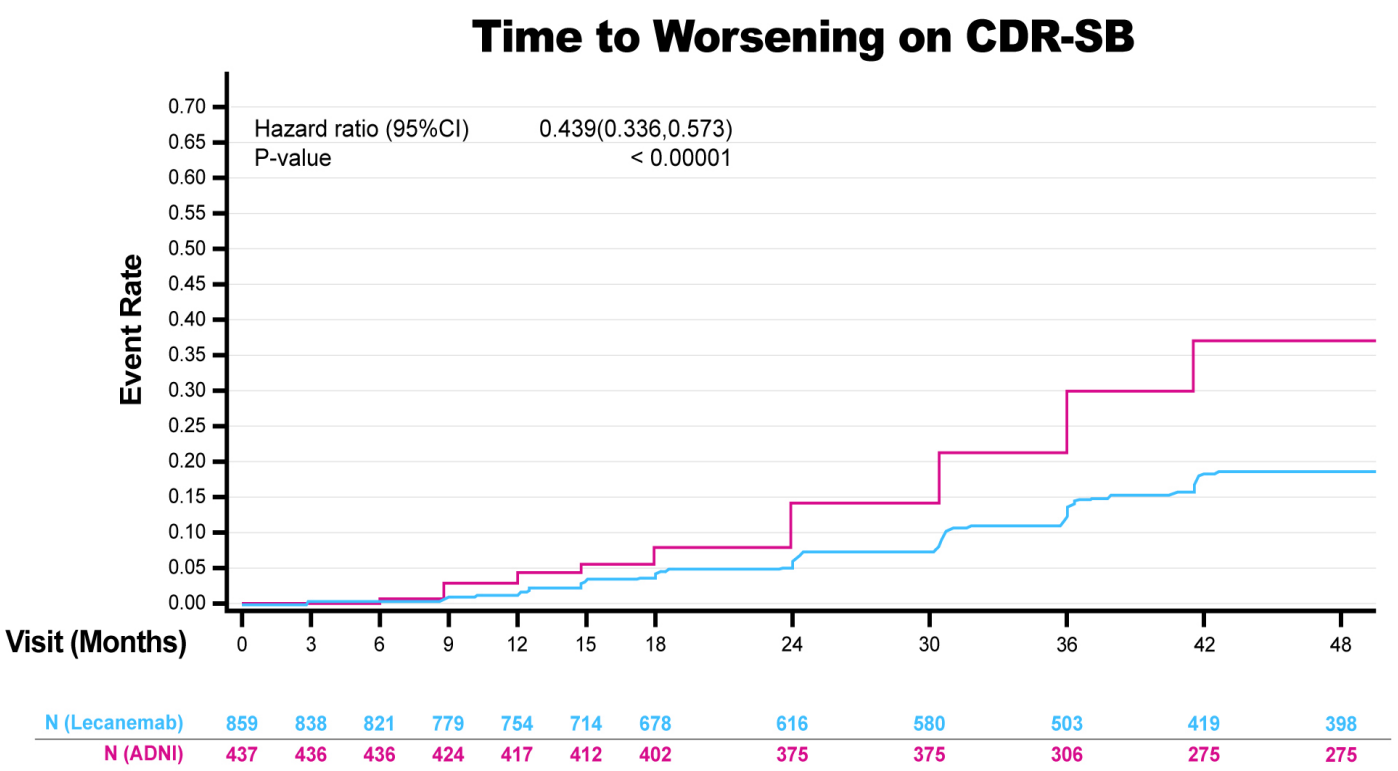
Based on modified intention-to-treat analysis population. Adjusted mean change from baseline, SE and p-value are derived using mixed model repeat measures (MMRM) with treatment group, visit, treatment group by visit interaction, clinical subgroup, use of Alzheimer’s disease symptomatic medication at baseline, ApoE4 carrier status, region, baseline value by visit interaction as fixed effects, and baseline value as covariate.

ADNI, Alzheimer's Disease Neuroimaging Initiative. CDR-SB, Clinical Dementia Rating-sum of boxes. OLE, open-label extension. SE, standard error.

Retard de progression vers le stade de démence à 48 mois

Quoi de plus pertinent cliniquement qu'une réduction du risque de démence ?

Le lecanemab réduit le RR de démence (modérée à sévère) de 56% vs ADNI



Van Dick C. AAIC, Toronto, Canada, July 2025.

Note: OLE includes those participants on subcutaneous and intravenous formulations.

ADNI, Alzheimer's Disease Neuroimaging Initiative. CDR-SB, Clinical Dementia Rating-sum of boxes.

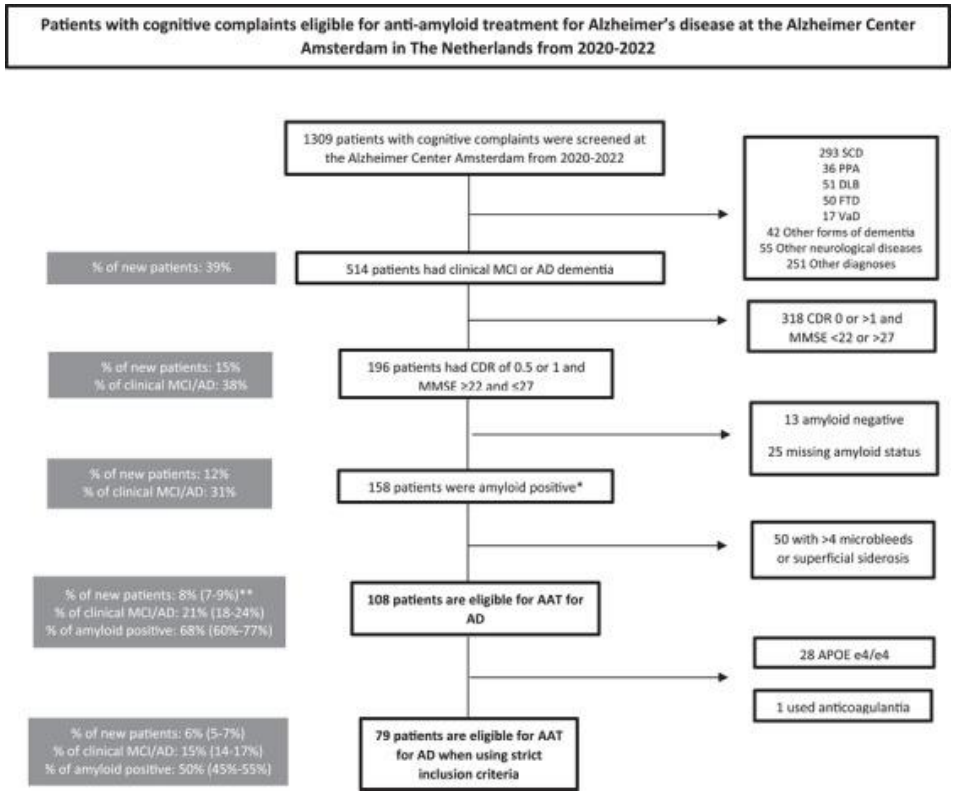
- Proportion de patients qui progressent vers le stade de démence
  - ADNI: 37.4%
  - Lecanemab: 18.6%

CDR-SB Range	Staging Category
0	Normal
0.5 – 4.0	Questionable Cognitive Impairment
0.5 – 2.5	Questionable Impairment
3.0 – 4.0	Very Mild Dementia
4.5 – 9.0	Mild Dementia
9.5 – 15.5	Moderate Dementia
16.0 – 18.0	Severe Dementia

- Progression was defined as CDR-SB Score progressing to moderate dementia (9.5-15.5) or severe dementia (16.0-18.0) based on dementia staging on CDR-SB (O'Bryant et al., Arch Neurol 2008)
- Given less frequent assessment, since controlled-based imputation was used for missing data in this analysis, CDR-SB (which has greater range) was used rather than global CDR for disease staging

Eligibilité pour l’immunothérapie en pratique clinique

Un population restreinte qui réduit le problème de faisabilité ?



- Eligibilité basée sur l’approbation européenne
- 8 % des nouveaux patients et 21 % des patients avec un diagnostic clinique de MCI ou de MA (âge moyen – 63 ans)
- Résultats similaires dans d’autres centres : 8%

Claus JJ et al. Generalizability of trial criteria on amyloid-lowering therapy against Alzheimer's disease to individuals with mild cognitive impairment or early Alzheimer's disease in the general population. Eur J Epidemiol. 2025.
Eligibilité basée sur l’approbation européenne
Pittock RR et al. Eligibility for anti-amyloid treatment in a population-based study of cognitive aging. Neurology. 2023;101(19):e1837-e1849.

- Dans un centre gériatrique : 0,7%

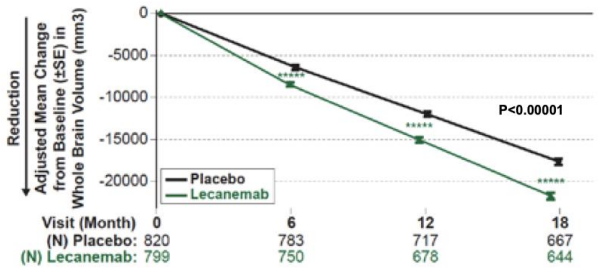
Canevelli M, Rossi PD, Astrone P, Consorti E, Vanacore N, Cesari M. “Real world” eligibility for aducanumab. J Am Geriatr Soc. 2021;69(10):2995-2998.

- Une éligibilité ne veut pas dire un traitement !

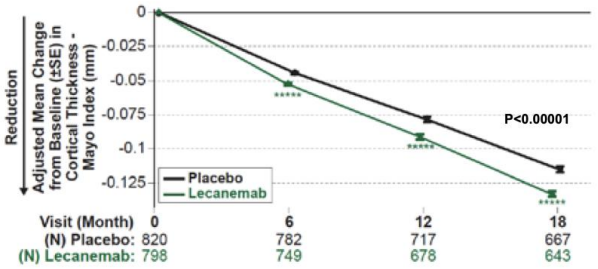
Vigneswaran S, Vijverberg EGB, Barkhof F, van de Giessen E, Lemstra AW, Pijnenburg Y, Teunissen CE, van der Flier WM, van Harten AC. "Real-world" eligibility for anti-amyloid treatment in a tertiary memory clinic setting. Alzheimers Dement. 2025 Jun;21(6):e70375.

Atrophie et Lécanémab

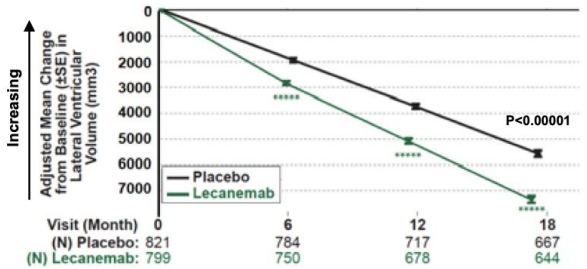
Whole brain volume



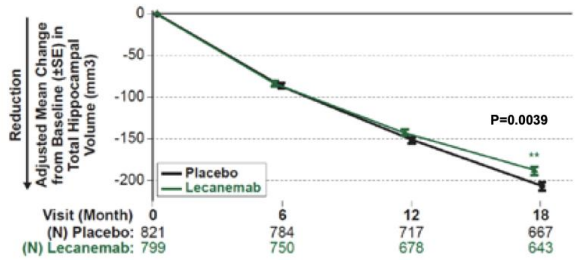
Cortical thickness



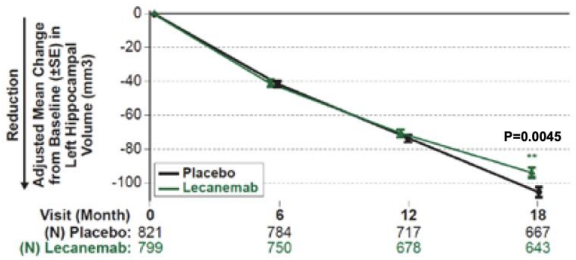
Lateral ventricular volume



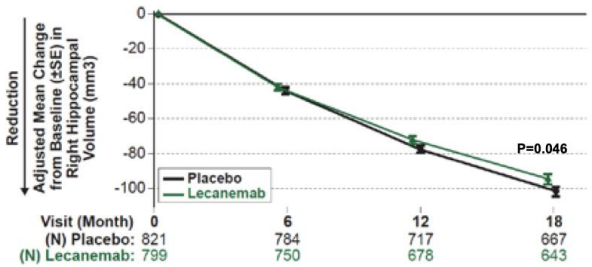
Total hippocampal volume



Left hippocampal volume



Right hippocampal volume



* P<0.05; ** P<0.01; *** P<0.001; **** P<0.0001

Alves F, Kalinowski P, Ayton S. Accelerated Brain Volume Loss Caused by Anti-β-Amyloid Drugs: A Systematic Review and Meta-analysis. Neurology. 2023 May 16;100(20):e2114-e2124.

CORRESPONDENCE · Volume 24, Issue 3, P189-190, March 2025 Download Full Issue

Amyloid-related iatrogenic atrophy of the brain: data transparency is an urgent safety priority

Scott Ayton [a] · Robert Howard [b] · Madhav Thambisetty [c]

Quelles explications ?

Pseudo-atrophie liée à l'élimination des dépôts amyloïdes ?

Belder CRS, Boche D, Nicoll JAR, Jaunmuktane Z, Zetterberg H, Schott JM, Barkhof F, Fox NC. Brain volume change following anti-amyloid β immunotherapy for Alzheimer's disease: amyloid-removal-related pseudo-atrophy. Lancet Neurol. 2024 Oct;23(10):1025-1034.

- Quantité totale de bêta-amyloïde insuffisante pour contribuer de manière significative à la variation de volume (environ 5ml/placebo)

Alves F, Kalinowski P, Ayton S. Accelerated Brain Volume Loss Caused by Anti-β-Amyloid Drugs: A Systematic Review and Meta-analysis. Neurology. 2023 May 16;100(20):e2114-e2124.

- Dissociation spatiale (perte de volume de la SB) et temporelle (atrophie continue à progresser au-delà de 12 mois et donc non en lien avec les ARIA)
- Phénomène également mis en évidence avec les inhibiteurs de la β-sécrétase

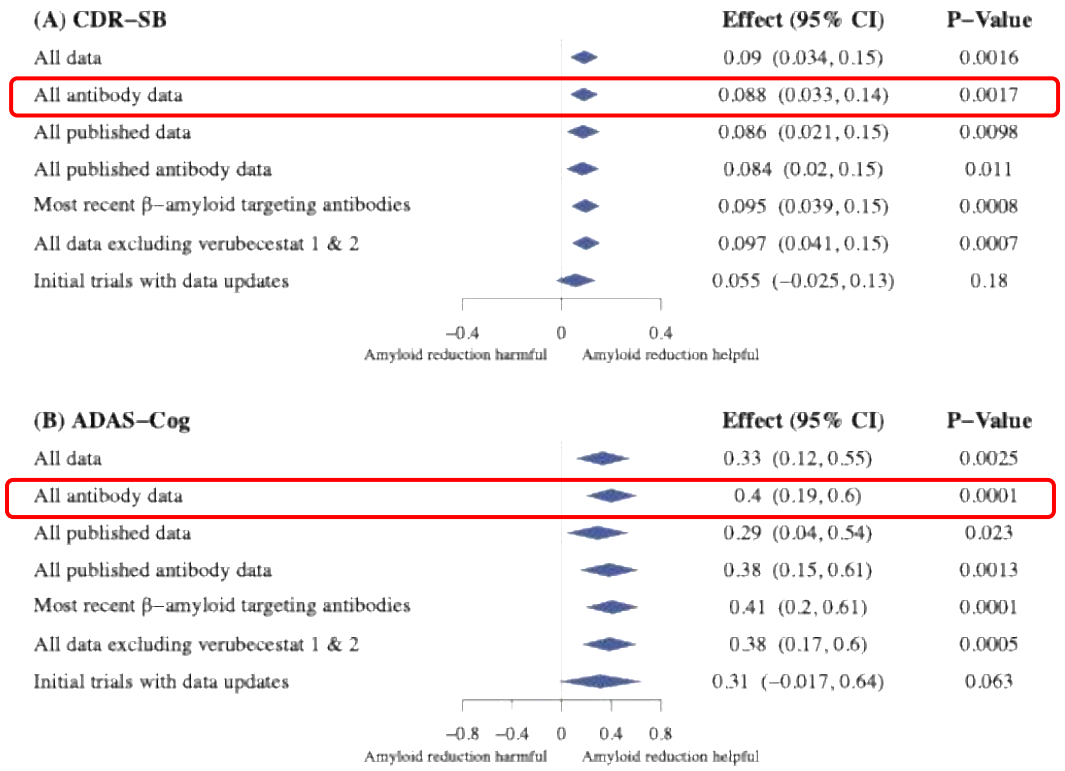
Inflammation comme mécanisme plausible ?

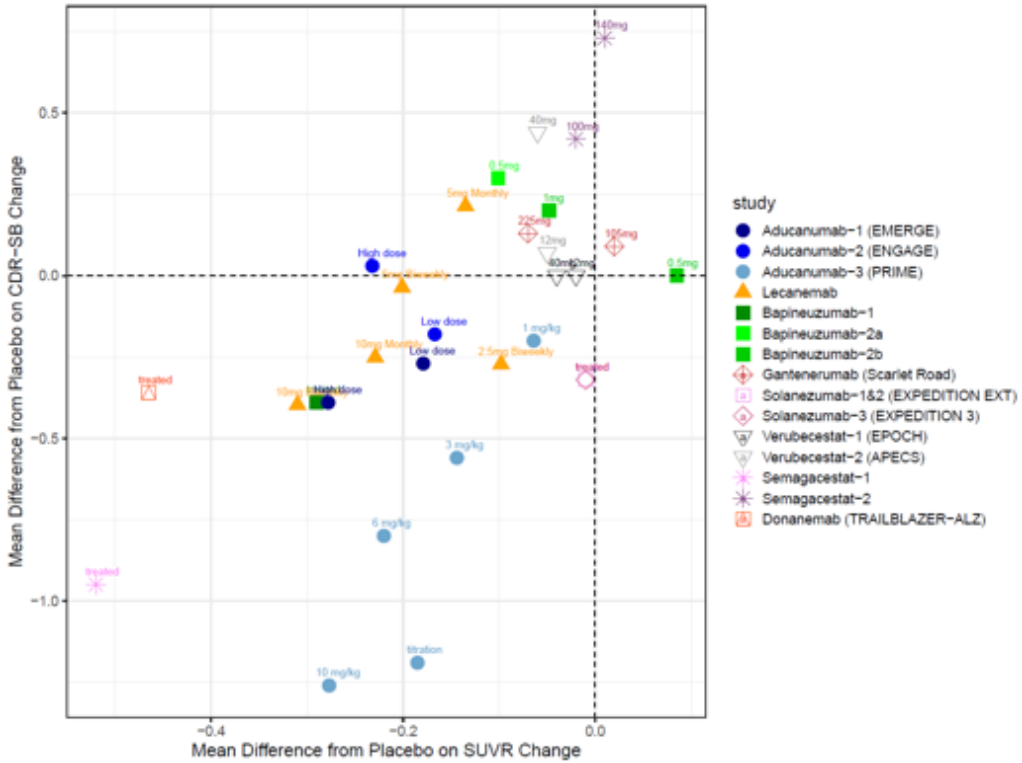
- Etude nécropsique d'un patient traité par aducanumab : activité microgliale intense autour des plaques chez les patients non traités/patient PRIME LTE

Plowey ED, Bussiere T, Rajagovindan R, Sebalusky J, Hamann S, von Hehn C, Castrillo-Viguera C, Sandrock A, Budd Haeberlein S, van Dyck CH, Huttner A. Alzheimer disease neuropathology in a patient previously treated with aducanumab. Acta Neuropathol. 2022 Jul;144(1):143-153.

Neurodégénéresence ? Aucun lien établi avec le déclin cognitif et les ARIA !

Relation entre la clairance amyloïde et l'effet cognitif





- Randomisation comme variable instrumentale pour éliminer biais de confusion
- Ajout des études PRIME, TRAILBLAZER-ALZ, …

Pang M, Zhu L, Gabelle A, Gafson AR, Platt RW, Galvin JE, Krolak-Salmon P, Rubino I, de Moor C, Belachew S, Shen C. Effect of reduction in brain amyloid levels on change in cognitive and functional decline in randomized clinical trials: An instrumental variable meta-analysis. Alzheimers Dement. 2023 Apr;19(4):1292-1299.

Pendant ce temps-là, dans le reste du monde…

Site		Référence	Taille d'échantillon (n=)	APOE4 homozygote (%)	ARIA (%)	ARIA-E (%)	ARIA-H isolée (%)	ARIA symptomatique (%)	ARIA sévère (%)
États-Unis	Washington	Paczynski et al, JAMA Neurol 2025	234	8,5	22	15	6,7	5,7	1
	Denver	Moon et al, Neurology 2025	44	11	9	2,3	4,6	2,3	2,3
	Abington	Weisman et al, Neurology 2025	95	12		7	2	-	-
	Louisville	Shields et al, JPAD 2024	71	13	24	18	10	18	4
Israel, Tel-Aviv**		Bregman et al, Alzeimers Res ther 2025	86	0	22,6	-	-	1,2	0*
Japon		Iwatsubo et al, CTAD 2024	148	-	6,5	-	-	-	-

*Une ARIA-E et H modéré chez patient hétérozygote APOE4 (confusion résolutive en 1 semaine)
**ARIA non lié au déclin cognitif

Et bien d'autres cohortes chinoises de plus grande envergure non encore publiées !

Paczynski M, Hofmann A, Posey Z, Gregersen M, Rudman M, Ellington D, et al. Lecanemab Treatment in a Specialty Memory Clinic. JAMA Neurol. 2025 July 1;82(7):655–65.
Bregman N, Nathan T, Shir D, Omer N, Levy MH, David AB, et al. Lecanemab in clinical practice: real-world outcomes in early Alzheimer's disease. Alzheimers Res Ther. 2025 May 28;17(1):119.

Forme sous-cutanée et dose de maintenance

FDA Approves LEQEMBI® (lecanemab-irmb) IV Maintenance Dosing for the Treatment of Early Alzheimer’s Disease

January 26, 2025

Once every four weeks maintenance dosing may be easier for patients and care partners to continue treatment

Alzheimer's disease progression does not stop after plaque clearance; ongoing treatment with LEQEMBI can slow disease progression and prolong the benefits of therapy

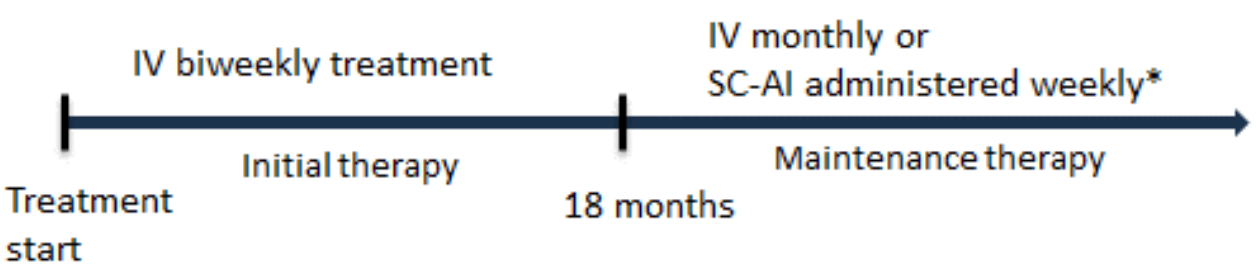


Image of transition from initial therapy to SC-AI maintenance therapy

*Application for SC-AI maintenance therapy is under US FDA review.

FDA Approves LEQEMBI® IQLIK™ (lecanemab-irmb) Subcutaneous Injection for Maintenance Dosing for the Treatment of Early Alzheimer’s Disease

LEQEMBI IQLIK is the first and only anti-amyloid treatment to offer an at-home injection to help patients and care partners continue to treat this progressive, relentless disease after initial treatment of 18 months
LEQEMBI IQLIK will be launched on October 6, 2025, in the U.S.

FDA U.S. FOOD & DRUG ADMINISTRATION

FDA to recommend additional, earlier MRI monitoring for patients with Alzheimer’s disease taking Leqembi (lecanemab)

Earlier monitoring can potentially help identify patients experiencing brain swelling or fluid buildup and help inform treatment decision-making

Quid de la France dans la recherche clinique actuelle ?

- Rapport de la HAS : 3,3% des patients inclus français…
- En 2024 : 140
- Nécessité d’une recherche thérapeutique forte académique et industrielle +++

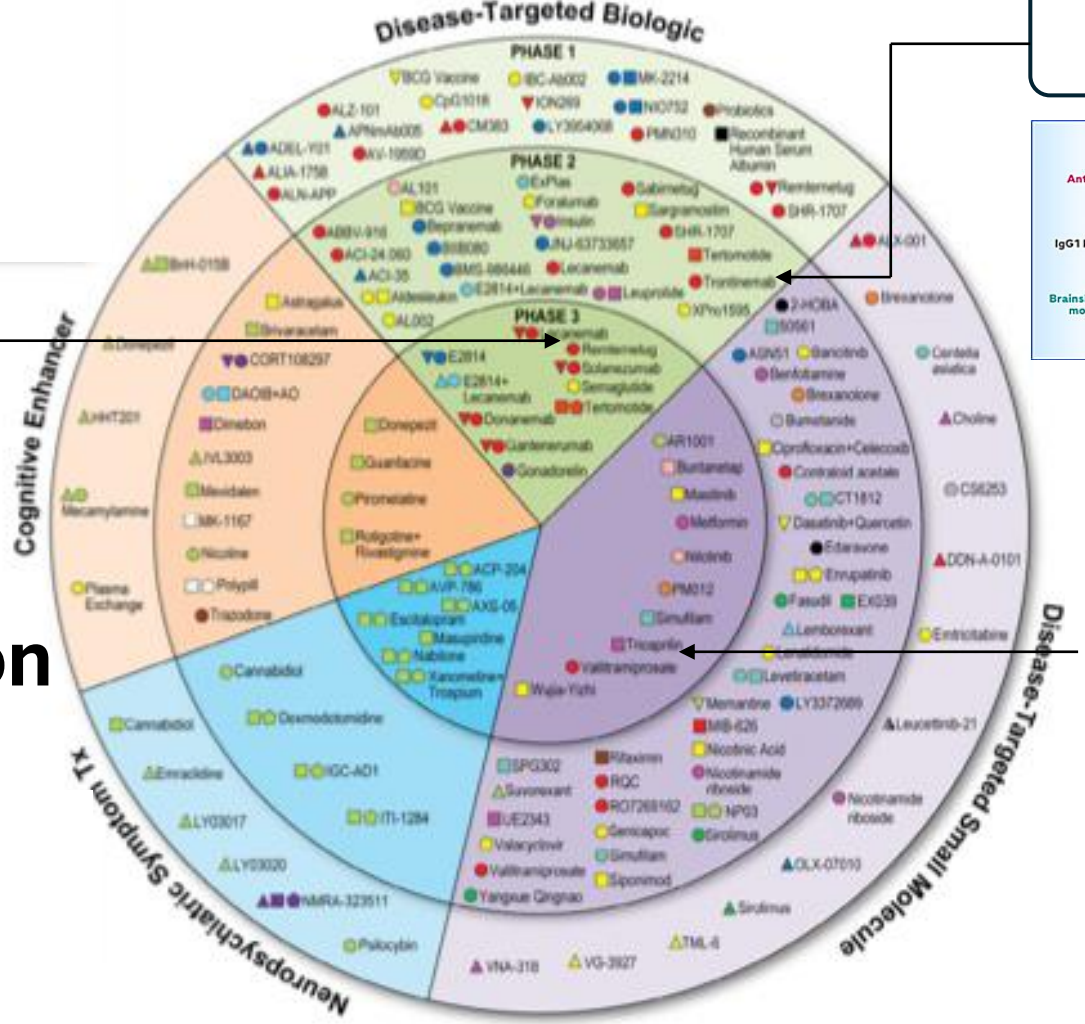
REMTERNETUG

Anticorps monoclonal anti-amyloïde ciblant l'Aß pyroglutamate

Phase III TRAILRUNNER-ALZ 3 : IV/12 semaines
Phase III TRAILRUNNER-ALZ 2 : SC/semaine

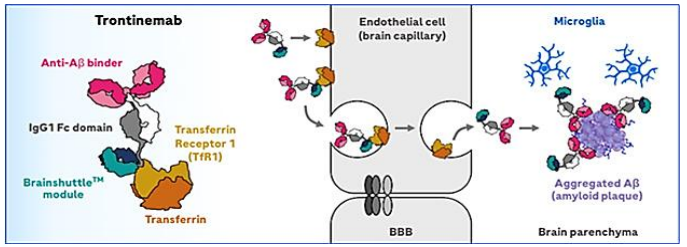
Lilly

La nouvelle génération des thérapies anti-amyloïdes



TRONTINEMAB

Technologie Brainshuttle

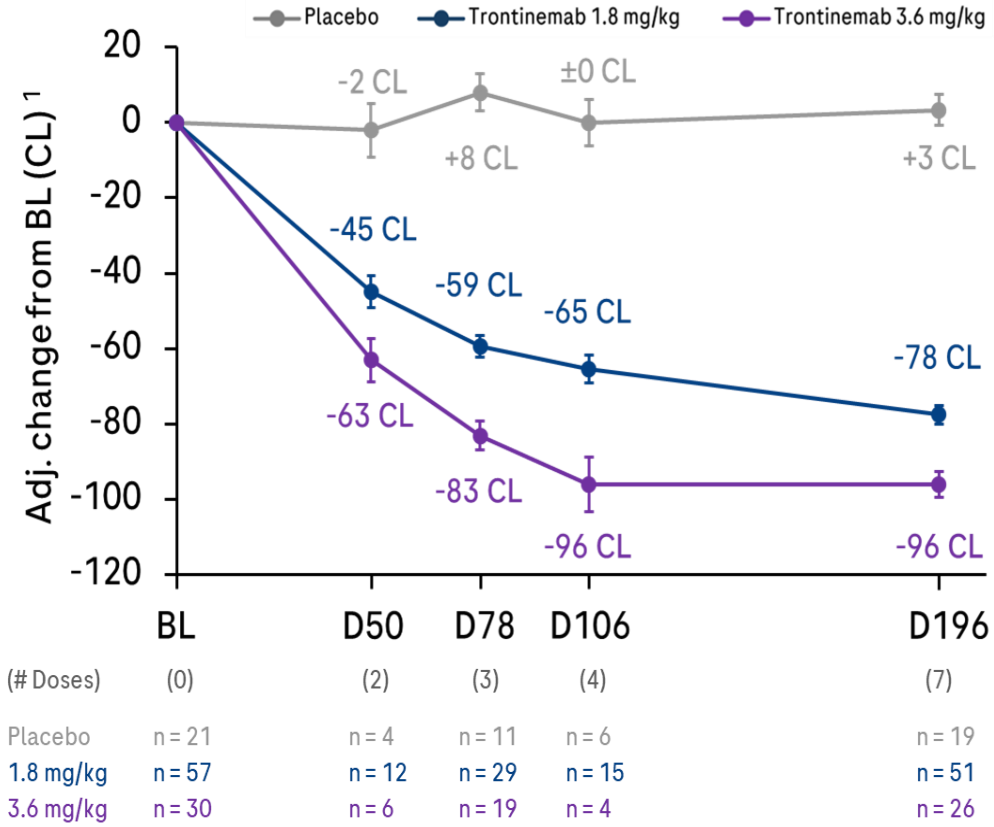


Roche

Cummings JL, Zhou Y, Lee G, Zhong K, Fonseca J, Leisgang-Osse AM, Cheng F. Alzheimer's disease drug development pipeline: 2025. Alzheimers Dement (N Y). 2025 Jun 3;11(2):e70098. doi: 10.1002/trc2.70098. PMID: 40463637; PMCID: PMC12131090.

Effet du Trontinémab sur la charge amyloïde

Résultats de l’étude de phase Ib/IIb parties 1 + 2 combinées



Participants ≤24 CL (%)	1.8 mg/kg (Part 1+2)	3.6 mg/kg (Part 1+2)
BL	0/61 (0%)	0/31 (0%)
D50	1/12 (8%)	1/6 (17%)
D78	12/29 (41%)	11/19 (58%)
D106	4/15 (27%)	4/4 (100%)
D196	33/51 **(65%)**	21/26 **(81%)**

p<0.0001 versus Placebo for both active dose groups and all post-BL time points via mixed model repeated measures (MMRM)

1. Kulic L, et al. presented at AD/PD 2025. 2. Values at each time point were based on an MMRM model, with change from baseline in amyloid PET burden (CL) as the dependent variable and with fixed effects of treatment group, categorical visit, treatment-by-visit interaction and baseline amyloid PET. 'n' represents the number of participants contributing to the model with available change from baseline at each visit. BL, baseline; CL, centiloid; D, day; PET, positron emission tomography.

ARIA et Trontinémab

	PART 1 (n = 32)		PART 2 (n = 82)		PART 1 + 2 (COMBINED) (n = 114)	
Total number of participants with event (%)	**Cohort 3 1.8 mg/kg or Pbo (n = 16)**	**Cohort 4 3.6 mg/kg or Pbo (n = 16)**	**Cohort 3 1.8 mg/kg or Pbo (n = 60)**	**Cohort 4 3.6 mg/kg or Pbo (n = 22)**	**Cohort 3 1.8 mg/kg or Pbo (n = 76)**	**Cohort 4 3.6 mg/kg or Pbo (n = 38)**
ARIA-E[2]	1 (6.3%)	0	2 (3.3%)	0	**3 (3.9%)**	**0**
ARIA-H	1 (6.3%)	0	4 (6.7%)	1 (4.5%)	**5 (6.6%)**	**1 (2.6%)**
Microhaemorrhage	0	0	2 (3.3%)	1 (4.5%)	**2 (2.6%)**	**1 (2.6%)**
Superficial siderosis	1 (6.3%)	0	2 (3.3%)	0	**3 (3.9%)**	**0**
Concurrent ARIA-E + ARIA-H	0	0	0	0	**0**	**0**

Essais cliniques de phase III TRONTIER 1 et 2

ARIA-E, Amyloid-Related Imaging Abnormalities-Edema/Effusion. ARIA-H, Amyloid-Related Imaging Abnormalities-Microhemorrhages and Hemosiderin deposition. D, day; Pbo, placebo; Radiologic ARIA-E severity according to 5-point grading scale (Bracoud et al. Alzheimers Dementia 2017). 1. Kulic L, et al. presented at AD/PD 2025. Blinded safety data by dosing cohorts (cut-off date: 14 November 2024). The study remains ongoing and blinded to individual treatment assignments (randomization active to placebo 4:1 in both Part 1 and 2). Participants receiving trontinemab and placebo in a respective dose cohort are presented together by dosing cohort to avoid unblinding. 2. One participant in cohort 3 Part 1 developed two episodes of ARIA-E: first, on routine Day 22 MRI scan, radiographically mild, temporally associated with mildly impaired attention over approximately one week, complete radiographic resolution within 4 weeks; second, on routine on Day 281 MRI, radiographically mild+, asymptomatic, complete radiographic resolution within 8 weeks. In cohort 3 Part 2, one participant developed a mild+ asymptomatic ARIA-E on routine Day 22 MRI, another participant developed a mild ARIA-E on routine Day 78 MRI. Both ARIA-E events in Part 2 resolved within 4 weeks.

Pour finir

- En attente SMR
- Des preuves d’efficacité
- Une nouvelle vague dont l’objectif est d’optimiser
- « Ca prendra le temps que cela prendra mais ca arrivera »