Les immunothérapies anti-amyloides dans la maladie d'Alzheimer
Quoi de neuf ?

Pr Vincent Planche

Centre Mémoire Ressources Recherche, CHU de Bordeaux
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Liens d'intérêts

Au cours des 3 dernières années, investigateur ou co-investigateur local (non rémunéré): Evoke et Evoke+ (NCT04777396, NCT04777409, NovoNordisk), Embark (NCT03352527, NCT04241068, NCT05310071 Biogen), Lucidity (NCT03446001, TauRx Pharmaceuticals), Autonomy (NCT04619420, Janssen), INFRONT-3 (NCT 04374136, Alector).

Aucune rémunération, ni financement direct ou indirect de la part de l'industrie pharmaceutique.

Où s'était-on laissé l'an dernier ?

Deux essais de phase 3 positifs !

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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

Research

JAMA | Original Investigation

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

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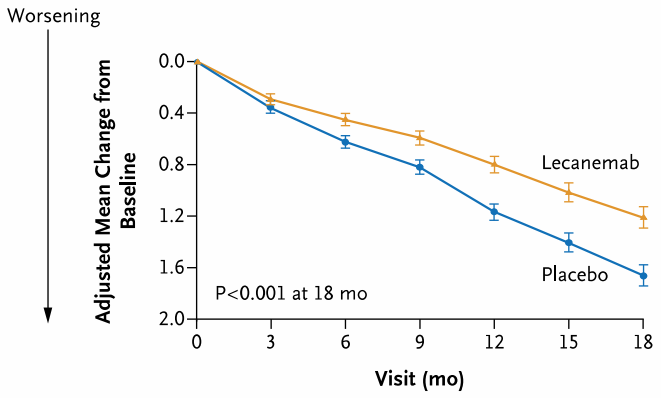
26 juillet 2024: pas d'AMM européenne

22 aout 2024: marché britannique (MHRA) mais de remboursement (NICE)

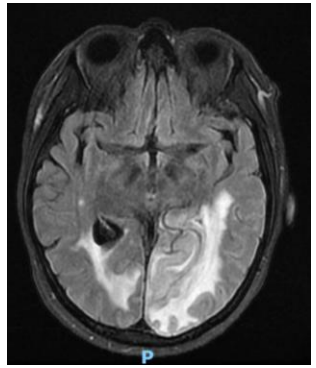
Pourquoi des décisions différentes ?

FDA U.S. FOOD & DRUG ADMINISTRATION

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH



Van Dyck et al., NEJM 2023



Avant ARIA
MMSE = 25/30

1 an après ARIA
MMSE = 16/30

Villain, Planche & Levy, Rev Neurol, 2022

Pourquoi des décisions différentes ?

Black box warning: 

WARNING: AMYLOID RELATED IMAGING ABNORMALITIES (ARIA)

- Monoclonal antibodies directed against aggregated forms of amyloid beta, including LEQEMBI, can cause amyloid related imaging abnormalities (ARIA), characterized as ARIA with edema (ARIA-E) and ARIA with hemosiderin deposition (ARIA-H). Incidence and timing of ARIA vary among treatments. ARIA usually occurs early in treatment and is usually asymptomatic, although serious and life-threatening events rarely can occur. Serious intracerebral hemorrhages >1 cm, some of which have been fatal, have been observed in patients treated with this class of medications.
  - Apolipoprotein E ε4 (ApoE ε4) Homozygotes: Patients who are ApoE ε4 homozygotes (approximately 15% of Alzheimer's disease patients) treated with this class of medications, including LEQEMBI, have a higher incidence of ARIA, including symptomatic, serious, and severe radiographic ARIA, compared to heterozygotes and noncarriers. Testing for ApoE ε4 status should be performed prior to initiation of treatment to inform the risk of developing ARIA. Prior to testing, prescribers should discuss with patients the risk of ARIA across genotypes and the implications of genetic testing results. Prescribers should inform patients that if genotype testing is not performed, they can still be treated with LEQEMBI; however, it cannot be determined if they are ApoE ε4 homozygotes and at higher risk for ARIA.
- Consider the benefit of LEQEMBI for the treatment of Alzheimer's disease and potential risk of serious adverse events associated with ARIA when deciding to initiate treatment with LEQEMBI

Overall, the CHMP considered that the benefits of treatment are not large enough to outweigh the risks associated with Leqembi. Therefore, it recommended refusing marketing authorisation in the EU.

Pourquoi des décisions différentes ?

Medicines & Healthcare products Regulatory Agency

The CHM therefore advised that the risk benefit of lecanemab was favourable in the patients who were ApoE4 non-carriers or heterozygous but not in the homozygous group, and that testing for the APOE4 gene should be carried out before treatment.

https://www.gov.uk/government/news

NICE National Institute for Health and Care Excellence

However, the costs of providing the treatment, including fortnightly infusions in hospital and intensive monitoring for side effects, combined with the relatively small benefits it provides to patients means it cannot be considered good value for the taxpayer, the independent NICE committee has said.

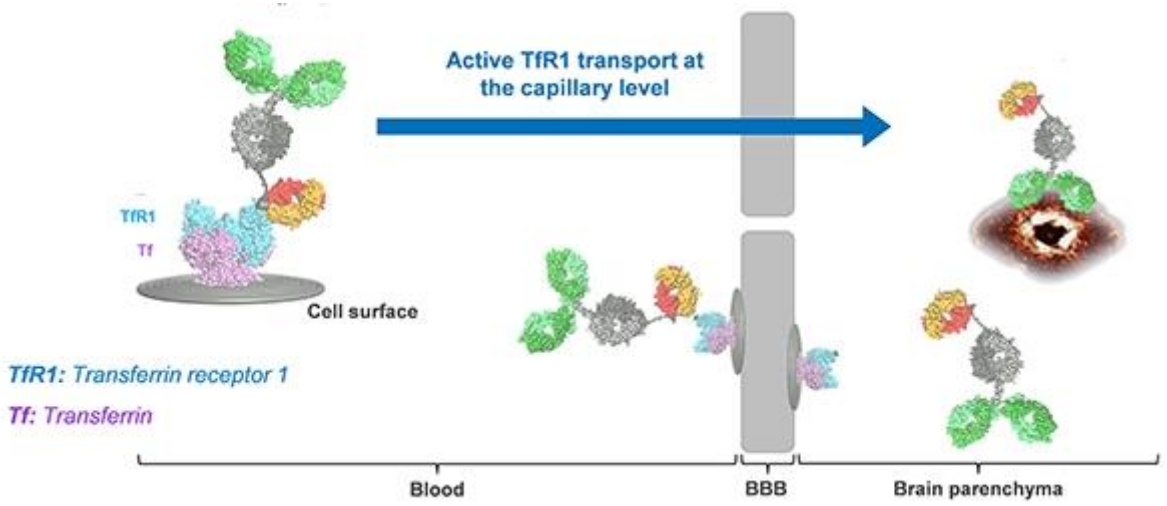
https://www.nice.org.uk/news

What next ?

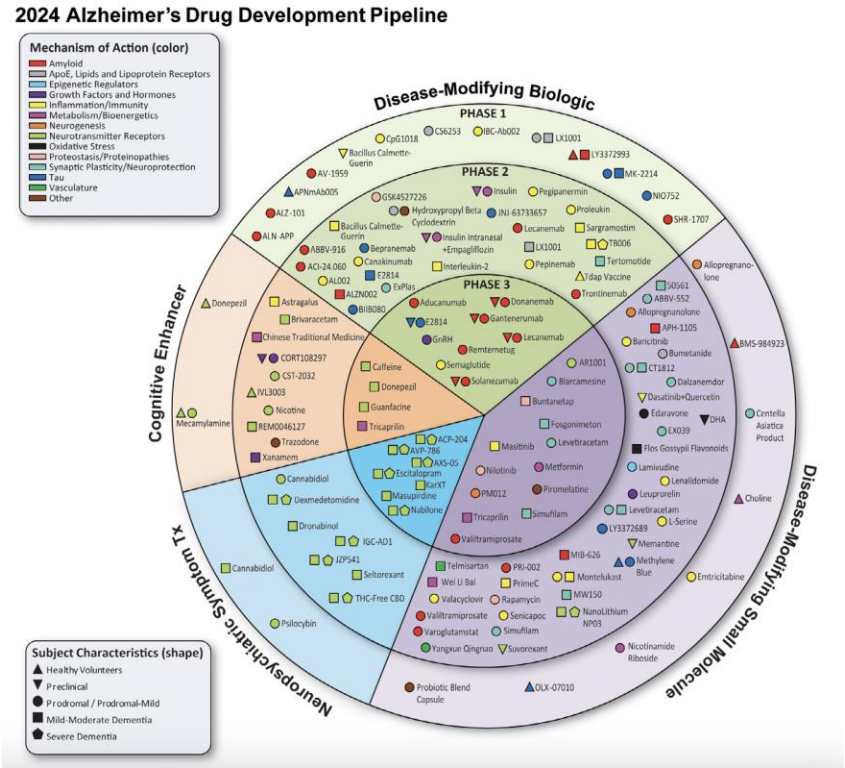
Les immunothérapies anti-amyloides et les autres

Diminuer les risques avec une même efficacité biologique?

Trontinemab (Roche) :



https://www.alzforum.org/news



Cumings et al., Alzheimer Dement (NY), 2024