Differences Between the Anti-Amyloid Drugs

Alzheimer's Quality Initiative

Lecanemab (Leqembi) and **Donanemab** (Kisunla) are both anti-amyloid medications developed and approved to treat Alzheimer's disease (AD). Both target amyloid-beta in the brain, clear it out and slow the progression of the disease. This translates into added 5-6 months slowing over 18-months. Both are monoclonal antibodies that make immune cells eat amyloid away from the brain. Both are infusion therapies that advance AD treatment.

They have important differences. Lecanemab targets protofibrils, tiny amyloid clumps and strands. Donanemab targets a form of amyloid-beta called N3pG found on amyloid plaques. While both therapies have a side effect called ARIA, for Amyloid Related Imaging Abnormalities, which primarily consists of swelling in the brain, their rates differ across a genetic variant called APOE. In order to make an informed decision about your health, it is important to know your APOE type.

% ARIA-E	LEC (896 Lec, 897 placebo)	DON (860 Don, 876 placebo)
Non-carrier	5.4% (0.3% placebo), 1.4% symptoms	15.7% (0.8% placebo) 3.9% symptoms
One APOE4	10.9% (1.9% placebo), 1.7% symptoms	22.6%, (1.9% placebo) 6.6% symptoms
APOE44	32.6% (3.8% placebo), 9.2% symptoms	40.6%, (3.4% placebo) 8.4% symptoms https://www.fda.gov/media/179166/download
Both drugs currently entail IV delivery and MRIs to look for ARIA. But the frequency differs. As does stopping criteria:		
Dosing	10 mg/kg every other week over one hour	700 mg every month X3, then 1400 mg Q month over ½ hour
MRIs	MRI prior to 1, 3, 5, 7, 14 dose. Then at 24.	MRI prior to 1, 2, 3, 4, and 7 dose. Then 12th, 18th.
Stop?	No firm stoppage criteria	Stop based on amyloid PET levels. Reduction defined as amyloid plaque levels<11 CL, or <25 CL on 2 PET scans (6, 12, 18 months) rates: 17%, 47%, and 69%. Simple visread neg rates: 30%, 70%, and 78%. No data after 1.5 years.
The drugs have different rates of infusion related reactions (fever, flu-like symptoms like chills, aches, nausea, BP changes).		
Infusion-related reactions	26% lec vs 7% placebo	9% don vs. 0.5% placebo