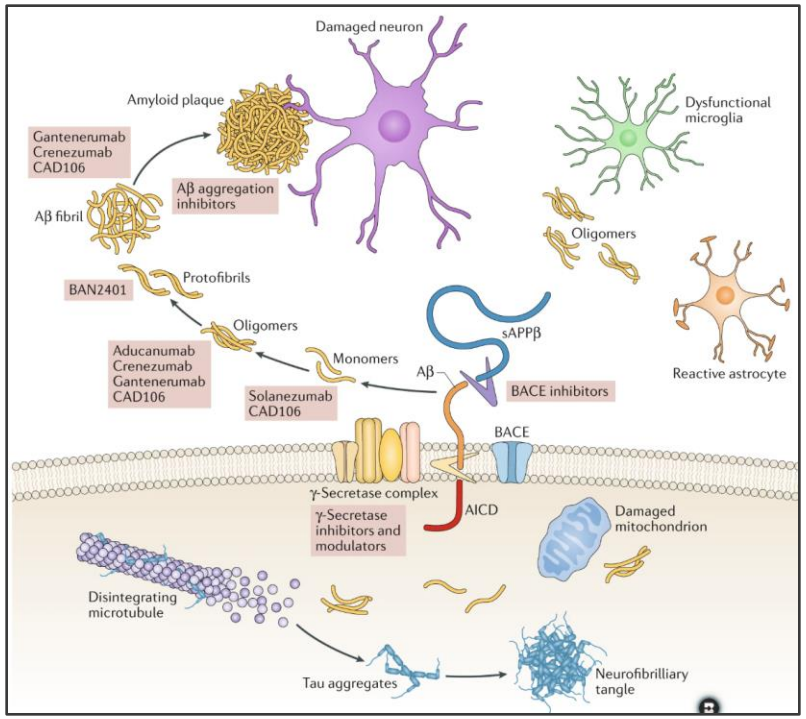
Alzheimer's Disease and Related Dementias: Advances and Off-Label Treatment Options

Anti-Amyloid Monoclonal Antibodies

Monoclonal Antibodies

- Disease modifying therapies for Alzheimer's disease that slow decline but are not curative
- Use for mild cognitive impairment or early-stage dementia due to Alzheimer's disease
- Each monoclonal antibody clears different amyloid aggregates by microglial phagocytosis
- Lecanemab (Leqembi®) targets protofibrils
- Donanemab (Kisunla™) acts on plaques
- Cholinesterase inhibitors and non-pharmacologic approaches should be continued in mild stage



(Panza et al, 2023)

Monoclonal Antibody Treatment

- **Infusions:** 1 x monthly for donanemab or 2 x monthly for lecanemab; likely 18 months
- **Requirement:** Early diagnosis; confirm presence of amyloid biomarkers with PET scan or cerebrospinal fluid
- **Basic exclusion criteria**
  - Anticoagulated or unable to undergo magnetic resonance imaging
  - Strict precautions to avoid anticoagulation during treatment

Monoclonal Antibody Treatment Risks

- Imaging abnormalities; brain swelling or bleeding
- Headache most common symptom; often clinically silent but can be fatal
- Symptoms can be stroke-like; must avoid anticoagulation
- Magnetic resonance imaging screening and surveillance required
- Risk increases with apolipoprotein E gene variant (APOEε4) number and cerebrovascular disease; highly recommended for risk stratification

Alert: Report monoclonal antibody use to alert for risk of brain hemorrhage

Options for Care Throughout the Disease Trajectory

MCI	Mild dementia	Moderate dementia	Severe dementia
Monoclonal antibodies if Alzheimer's disease present.			
	Acetylcholinesterase inhibitors*		
		Memantine*	
Supportive Care			

*consider stopping acetylcholinesterase inhibitors and memantine when disease severe

Anti-Amyloid Medications

Lecanemab and donanemab

- New monoclonal antibody medications against amyloid plaque given 1 – 2 times per month by IV infusion
- Approved for MCI or mild dementia due to Alzheimer's disease
- May slow progression of mild cognitive impairment by 4 to 6 months

(Sims, 2023 and Van Dyck, 2023)

Anti-Amyloid Medications

Eligibility:

- Alzheimer's disease documented by lumbar puncture or positron emission tomography (PET) scan
- Not on anticoagulation medications
- Not apolipoprotein E homozygous
- Patients must be in good health with controlled chronic conditions
- Able to tolerate serial MRIs to monitor for brain edema or bleeding

Note: With recent Food and Drug Administration approval, blood biomarkers are emerging as a relatively non-invasive option for detecting amyloid, but their role in routine diagnostic eligibility workup for anti-amyloid therapy is evolving

(Sims, 2023 and Van Dyck, 2023)