

## **AMYLOID IS A FALSE TARGET IN AD THERAPY**

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The following data support the concept that amyloid is a false target in AD therapy:

1. Heavy amyloid burden can be seen (PIB-PET and autopsy) in the brain of 30-40% normal elderly subjects with none or little cognitive impairment.
2. Most clinical data show a disconnection among level of a-beta in brain, neuronal and synaptic loss and dementia
3. Neuronal and synaptic loss and clinical symptoms correlate best with tau pathology
4. PIB-positive normal individual present no MRI evidence of atrophy
5. No clinical study has demonstrated that modifications of CSF a-beta levels correlate with modification of clinical outcomes.
6. Numerous Phase II and III clinical trials directed to: reduce production, facilitate clearance or prevent aggregation of a-beta have failed to show clinical benefits.
7. Inhibiting gamma secretase (Semagacestat trial) made AD patients worst!
8. Long-term follow up of 80 immunized patients showed no evidence of beneficial effects in terms of survival or time to severe AD
9. Passive or active immunization against a-beta may result in an almost complete removal in certain brain regions but does not prevent cognitive decay

Conclusion: a-beta may be associated to AD but a causal relation has not been demonstrated, therefore it does not constitute a real target for therapy.