Nature Reviews Neurology **7**, 657 (2011); doi:10.1038/nrneurol.2011.183

ALZHEIMER DISEASE

Amyloid-targeting antibody performs well in phase II trial

The fully human monoclonal antibody gantenerumab, which targets amyloid-β plaques, seems to cause a dose-dependent decrease in brain amyloid levels, according to a clinical trial involving 18 patients with mild to moderate Alzheimer disease (AD).

Accumulation of toxic amyloid plaques is a hallmark of the AD brain, and targeting of this process is a therapeutic strategy under investigation. In the current multicenter study, published in *Archives of Neurology*, patients were randomly assigned to receive placebo or monthly intravenous doses of gantenerumab (60 mg or 200 mg), which were administered for 2–7 months. PET scanning for the tracer carbon-11-labeled Pittsburgh compound B (^{11}C-PIB) was performed to measure regional brain amyloid levels at baseline and at the end of treatment.

Patients in the placebo group ($n = 4$) showed a mean 11% increase in cortical ^{11}C-PIB signal during the study. By contrast, the signal increased by an average of only 2.1% in patients receiving 60 mg gantenerumab ($n = 6$), and declined by 9.4% in patients in the 200-mg group ($n = 6$). The therapeutic antibody seems, therefore, to produce a dose-dependent reduction in plaque burden, although the small sample sizes preclude firm conclusions from being drawn.

In an *ex vivo* phagocytosis assay, live-cell imaging revealed that the drug dose-dependently increased microglial uptake of amyloid plaques within hours.

Future research should address whether targeting of amyloid levels translates into clinical benefit, and whether mild to moderate AD is a sufficiently early time point for starting treatment.

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Original article Ostrowitzki, S. *et al.* Mechanism of amyloid removal in patients with Alzheimer disease treated with gantenerumab. *Arch. Neurol.* doi:10.1001/archneurol.2011.1538