

# Alzheimer's Drugs Pipeline or Pipe dream?

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There are currently 546 clinical trials  
recruiting, underway or recently completed  
related to Alzheimer's disease

*[www.clinicaltrials.gov](http://www.clinicaltrials.gov)*

Currently available drugs treat cognitive symptoms

- Cholinesterase inhibitors (CI): **Aricept, Exelon, Razadyne**
- NMDA receptor inhibitor: **Namenda**

### **New study suggests:**

- modest long term slowing of disease progression from chronic use . . . especially when a CI and Namenda are combined

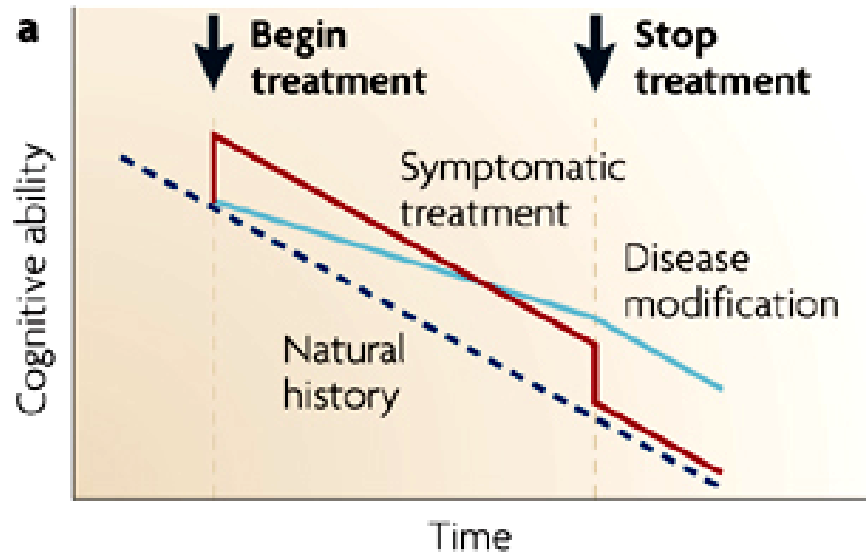
Treatment of psychiatric symptoms  
(agitation, anxiety, depression) include:

anti-depressants

anti-psychotics

good supportive care

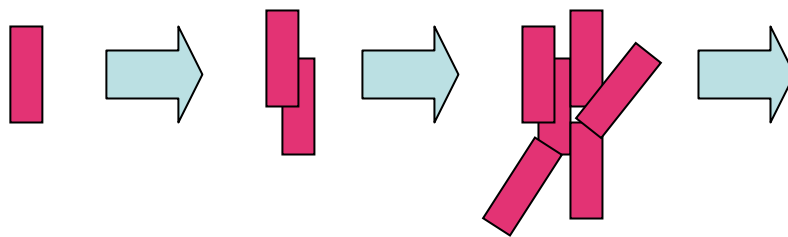
## Disease modification is a goal of newer drugs



# anti-amyloid drugs are on the horizon

## Amyloid peptides

## Amyloid plaque



QuickTime™ and a TIFF (Uncompressed) decompressor are needed to see this picture.

Aβ 40      Aβ 42



**Flurizan**

<http://www.rnw.nl/health/html/brain.html>

# Flurizan failure

- Drug is supposed to lower toxic forms of beta-amyloid
- Mechanism of drug was sound based on preclinical studies
- Too much hope based on smaller trials showing marginal success

Many questions remain unanswered: Did enough of the drug get to the brain? Did it affect beta-amyloid levels?

# Dimebon

Antihistamine drug from Russia

During 1980s was suggested to stimulate brain metabolism

Recent Phase 2 trial conducted in Russia was promising (183 patients)

Mechanism of action -unknown- but may affect brain cell survival by protecting mitochondria

QuickTime™ and a  
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*Doody, The Lancet, 2008*

A late stage clinical trial of Dimebon that will last 6 months is currently recruiting patients

[www.ConnectionStudy.com](http://www.ConnectionStudy.com)

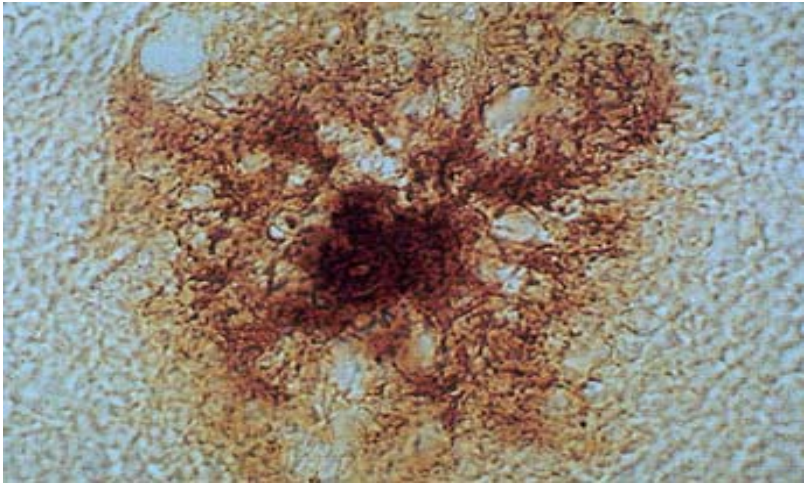
tel. no. 877-888-6386.

What do all these graphs and numbers really mean in terms of helping the patient?

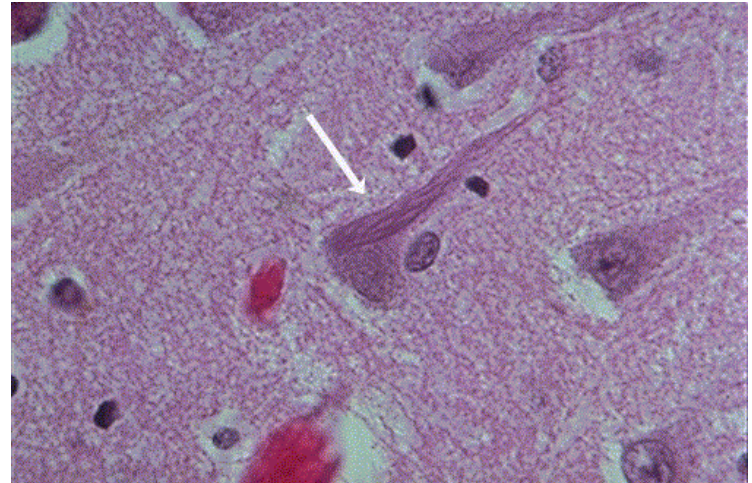
# Aricept vs placebo

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# Alzheimer's Disease Plaques and Tangles



$\beta$ -amyloid Plaques



Neurofibrillary Tangles

certain forms of beta-amyloid are toxic in the brain

beta-amyloid is believed to promote tau tangles

tau tangles are more closely correlated with cognitive decline

# Rember™

- Rember™ is a blue dye that dissolves tau tangles in a test tube
- Phase 2 clinical results are unpublished but were reported at ICAD summer 2008
- Patients treated with an intermediate dose of the dye remained stable for about a year and a half
- Brain imaging showed increased brain activity and blood flow in several areas of the brain known to be affected in Alzheimers'

## ***Caveat***

*This study may not have had proper controls  
--its conclusions may be called into question*

# PBT2

Claims to prevent build-up of toxic forms of beta-amyloid by binding to copper and zinc

May cause brain cells to absorb more copper needed for normal function

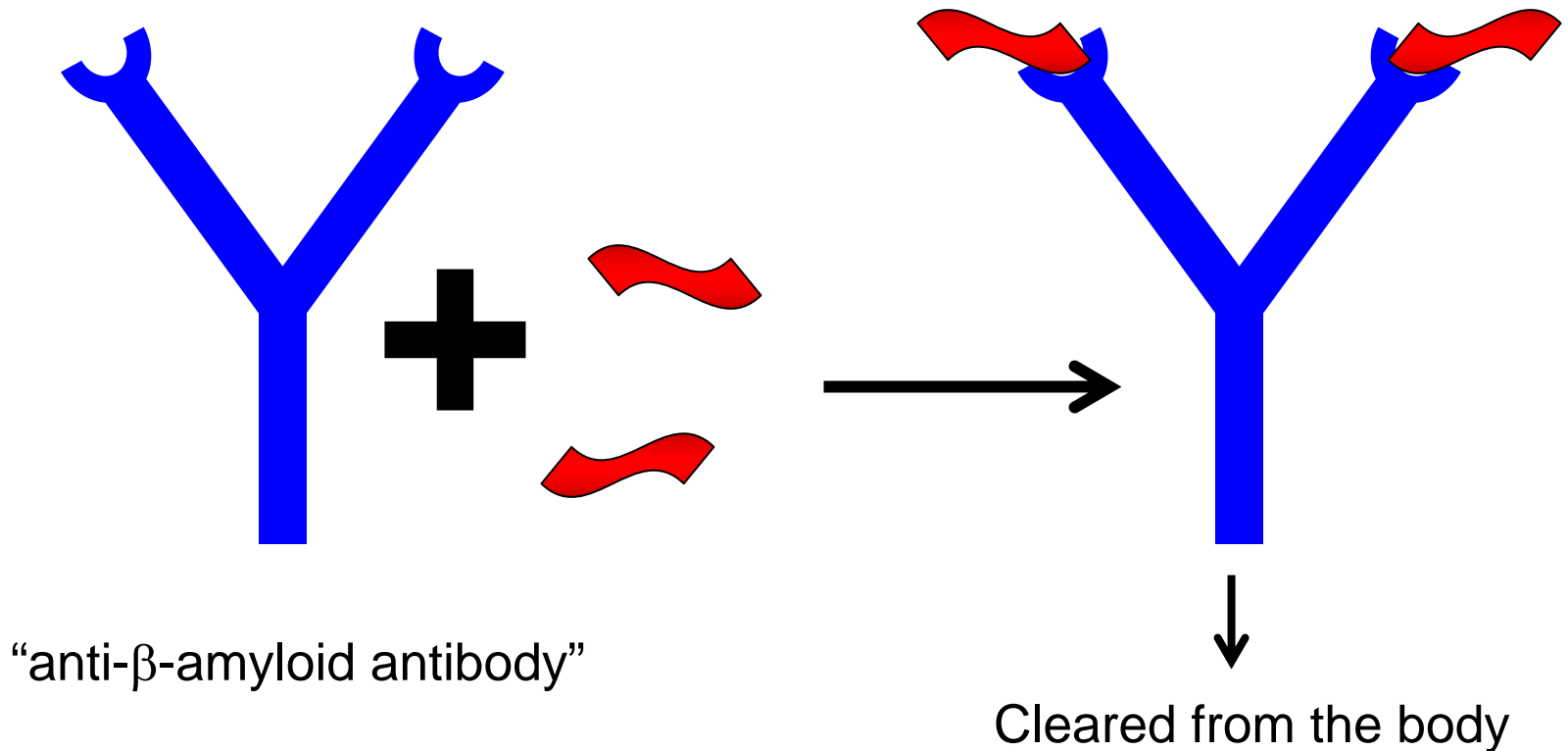
12 week Phase 2 trial showed some improvement in executive function and drop in beta-amyloid and tau levels

Preclinical study in Alzheimer model mice show rapid recovery of cognitive function

What is immunotherapy?

Its aim in treating AD is to reduce levels of beta-amyloid

**Antibodies** are protein molecules made in the body. They bind tightly to certain other molecules, in this case  $\beta$ -amyloid.



Bapineuzummab is an anti-beta-amyloid antibody that has recently shown some promise in a recently completed phase 2 trial

## Conclusions

Several new treatments are in, or are approaching, late stage clinical trials

Within 2 to 3 years we could know whether one or more of these treatments slow the progression of Alzheimer's

For more information about clinical trials  
visit

[alzinfo.org](http://alzinfo.org)

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