Effect on memory and attention of two doses of Memogain, a prodrug of galantamine, in healthy subjects

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INTRODUCTION

Alzheimer's Disease (AD) is the most common cause of dementia in the Western world. Cholinesterase inhibitors (ChEIs) have been shown to enhance cognitive functioning in patients with AD. The use of ChEIs and their maximum dose is limited by side effects, such as nausea, vomiting and diarrhoea. These side effects are caused by stimulation of peripheral ACh receptors. Memogain is a prodrug of galantamine that preferentially enters the CNS where it is cleaved to active galantamine. This proces is hypthesized to lead to higher concentrations of galantamine in the brain and lower concentrations in the peripheral circulation and therefore to fewer side effects and a higher degree of cognitive enhancement. In this first-in-human clinical study, safety, tolerability, pharmacokinetics (PK) and pharmacodynamics (PD) were assessed in healthy yound and healthy elderly subjects.

METHODS

This was a randomized, double-blind, double-dummy, placebo- and reference- controlled, dose-escalation study. Safety, PK and PD assessments were performed repeatedly after drug administration. PD was measured using a computerized test battery with various tests for memory, vigilance/arousal, subjective drug effects, eye movements and pharmaco-EEG.

Cohort	Treatment			Population
1	Memogain 5.5 mg (n=6)		placebo (n=2)	healthy young men
2	Memogain 11 mg (n=6)		placebo (n=2)	healthy young men
3	Memogain 22 mg (n=6)	galantamine 16 mg (n=6)	placebo (n=2)	healthy elderly men
4	Memogain 33 mg (n=6)	galantamine 16 mg (n=6)	placebo (n=2)	healthy elderly men
5	Memogain 44 mg (n=6)	donepezil 10 mg (n=6)	placebo (n=2)	healthy elderly men
Total N	30	18	10	Overall total: 58

RESULTS

- Memogain was well tolerated. Nausea en vomiting were reported more frequently in the galantamine group and in the 44mg Memogain group (fig. 4)
- Vigilance/arousal as measured using the adaptive tracker test improved after dosing of Memogain 33 and 44mg and donepezil 10 mg. This improvement was not observed after dosing of galantamine 16 mg (fig. 1, 2)
- Memogain had a significant effect on short term memory, which is greater than the effects of donepezil and galantamine (fig. 3)

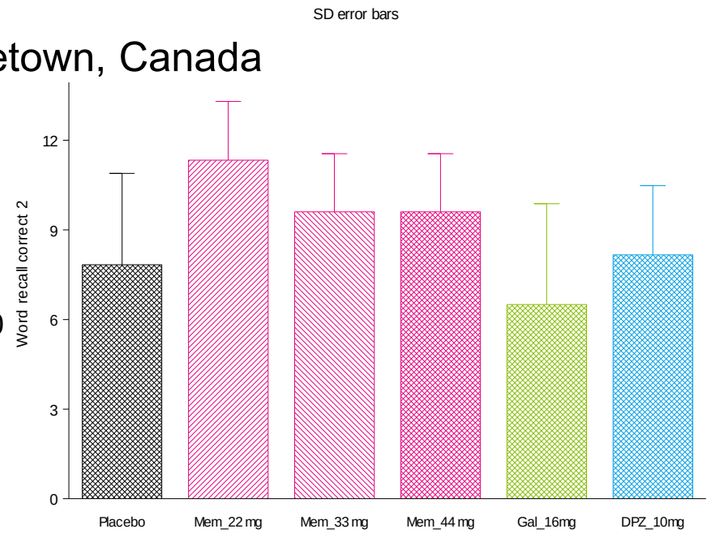

Figure 3: effect on short term memory

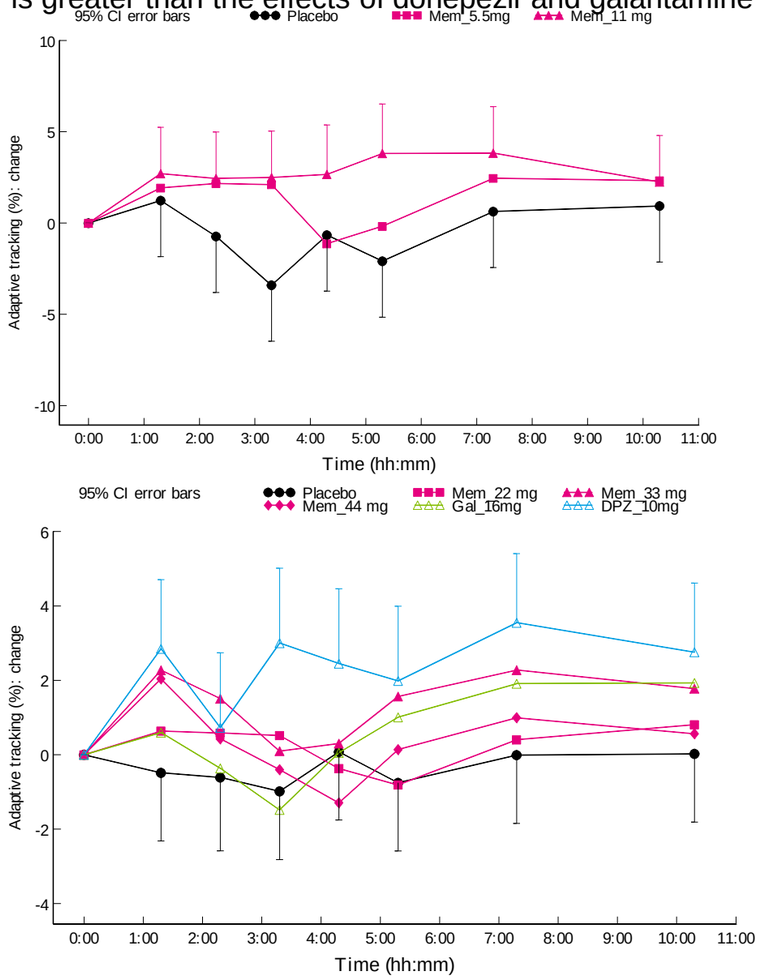

Figure 1 and 2: effect on attention

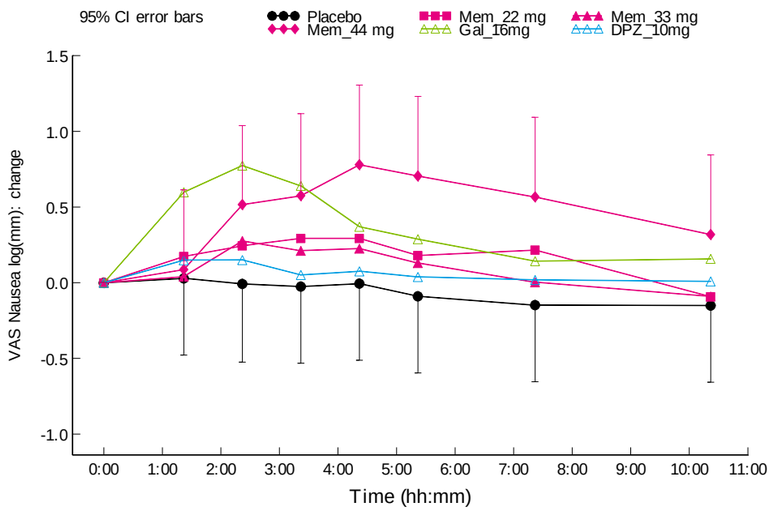

Figure 4: effect on VAS nausea

CONCLUSIONS

- A single dose of Memogain was well toleated up to doses of 44 mg.
- Single dosages of Memogain improved vigilance/arousal and short term memory in healthy young and elderly.
- Although Memogain appears to have an improved efficacy:safety ratio compared to galantamine, it's value in the treatment of patients with Alzheimer's Disease will have to be peformed in future clonical studies.

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