

Tolerability of Rapid Galantamine Titration in Patients Being Converted from Donepezil

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Background

- Acetylcholinesterase inhibitors (AChE-I) are currently indicated for the symptomatic treatment of cognitive decline associated with Alzheimer's disease (AD)
- Four FDA approved AChE-I
 - Tacrine-1993
 - Donepezil-1996
 - Rivastigmine-2000
 - Galantamine-2001
- Agents provide similar efficacy, yet differ in tolerability and pharmacokinetic properties

Background

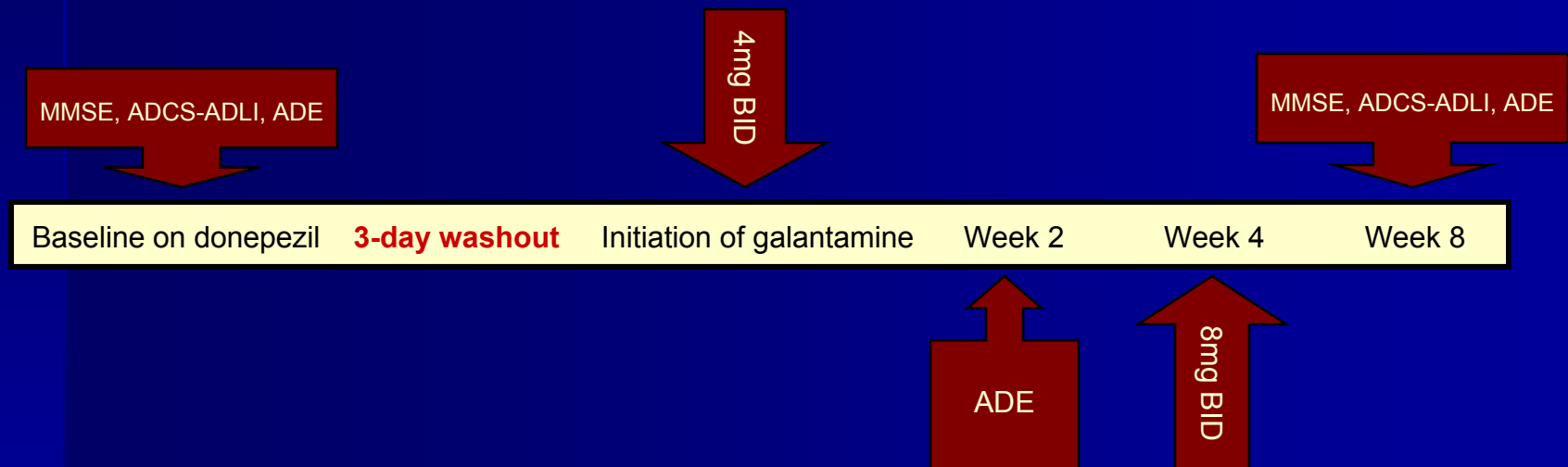
- Lexington Veterans Affairs Medical Center (LVAMC) offered donepezil as its formulary preferred AChE-I until Spring 2004 when it was replaced with galantamine
- In March 2005, the Pharmacy & Therapeutics Committee and the Clinical Education Board of the LVAMC approved a formulary therapeutic substitution of galantamine for donepezil in patients who were being maintained on donepezil
- To ensure an optimal transition of medication therapy, patients were followed by clinical pharmacists in a pharmacotherapy clinic

Methods

- Patients assessed for conversion upon refill request
- Patients assessed for eligibility
 - previous galantamine failure
 - allergy to galantamine
 - renal insufficiency
- Scheduled for baseline appointment

Methods

- Patients were initially converted according to the galantamine prescribing information (Phase I)

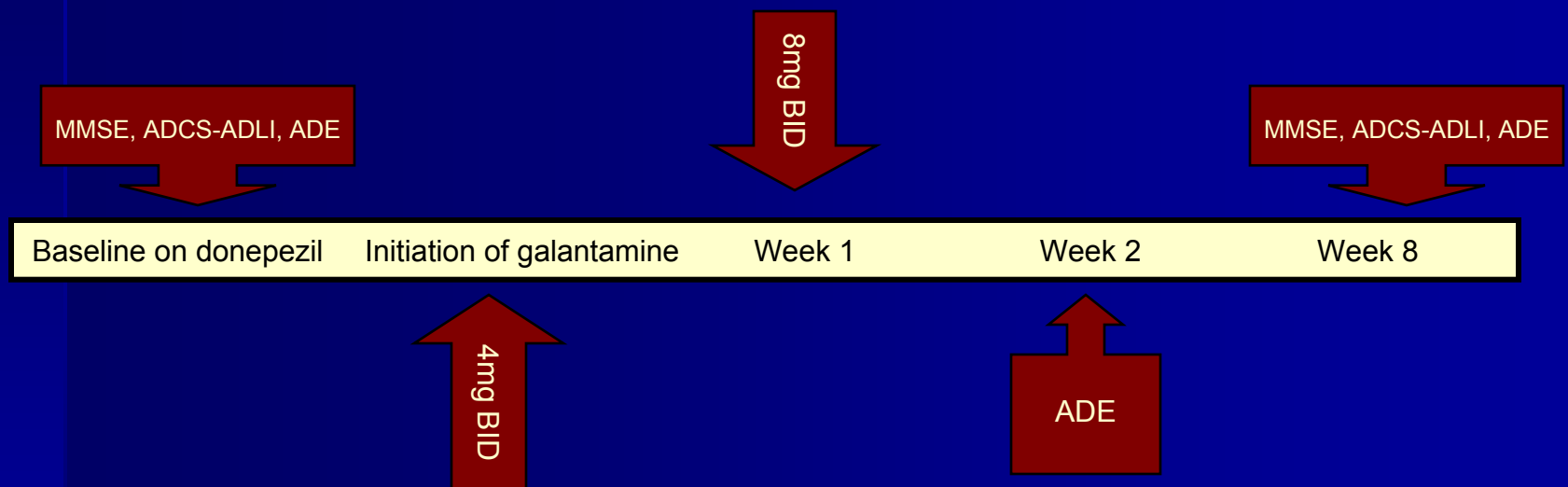


Methods

- Interim assessment
 - tolerability
 - efficacy
- Given risk of cognitive decline with slow titration, clinical pharmacy team decided to escalate the titration schedule

Methods

- Phase II of the conversion utilized an accelerated dosing escalation



Objective

- Evaluate the tolerability of two titration strategies of galantamine in patients being converted from donepezil therapy

Statistical Analysis

- Chi squared tests were used to determine differences in demographics and adverse effect scores between Phase I and Phase II subjects
- An odds ratio was calculated to determine differences in discontinuation rates between subjects in Phase I and Phase II

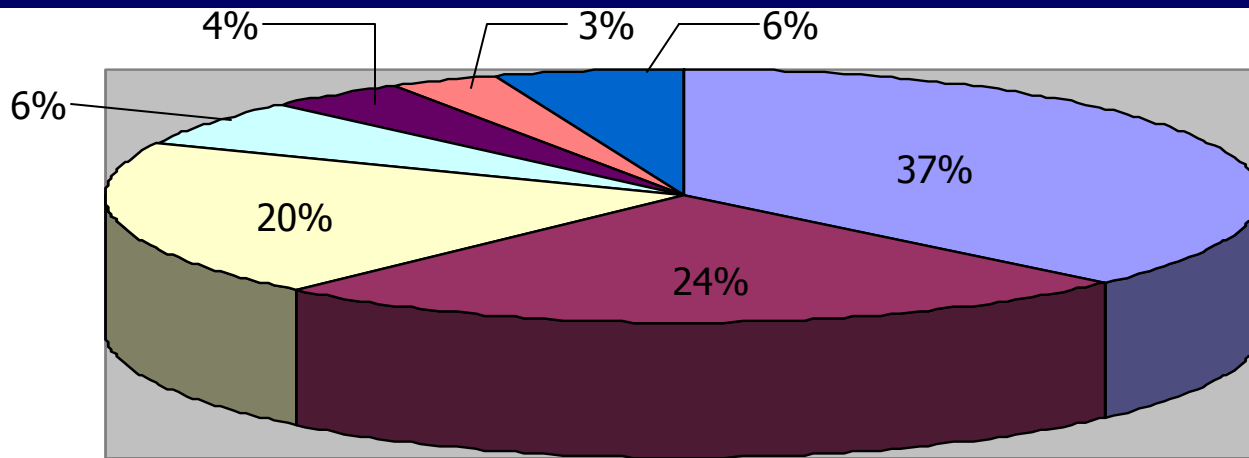
Patient Demographics

- One hundred thirty-one of 177 patients stable on donepezil were eligible for conversion to galantamine (74%)
 - Five patients were lost to follow-up after conversion
 - One hundred twenty-six patients evaluated
 - 68 in Phase I
 - 58 in Phase II
- At the conclusion of the eight-week follow-up period, 99/126 (76%) of those patients who were converted to galantamine remained on the medication

Patient Demographics

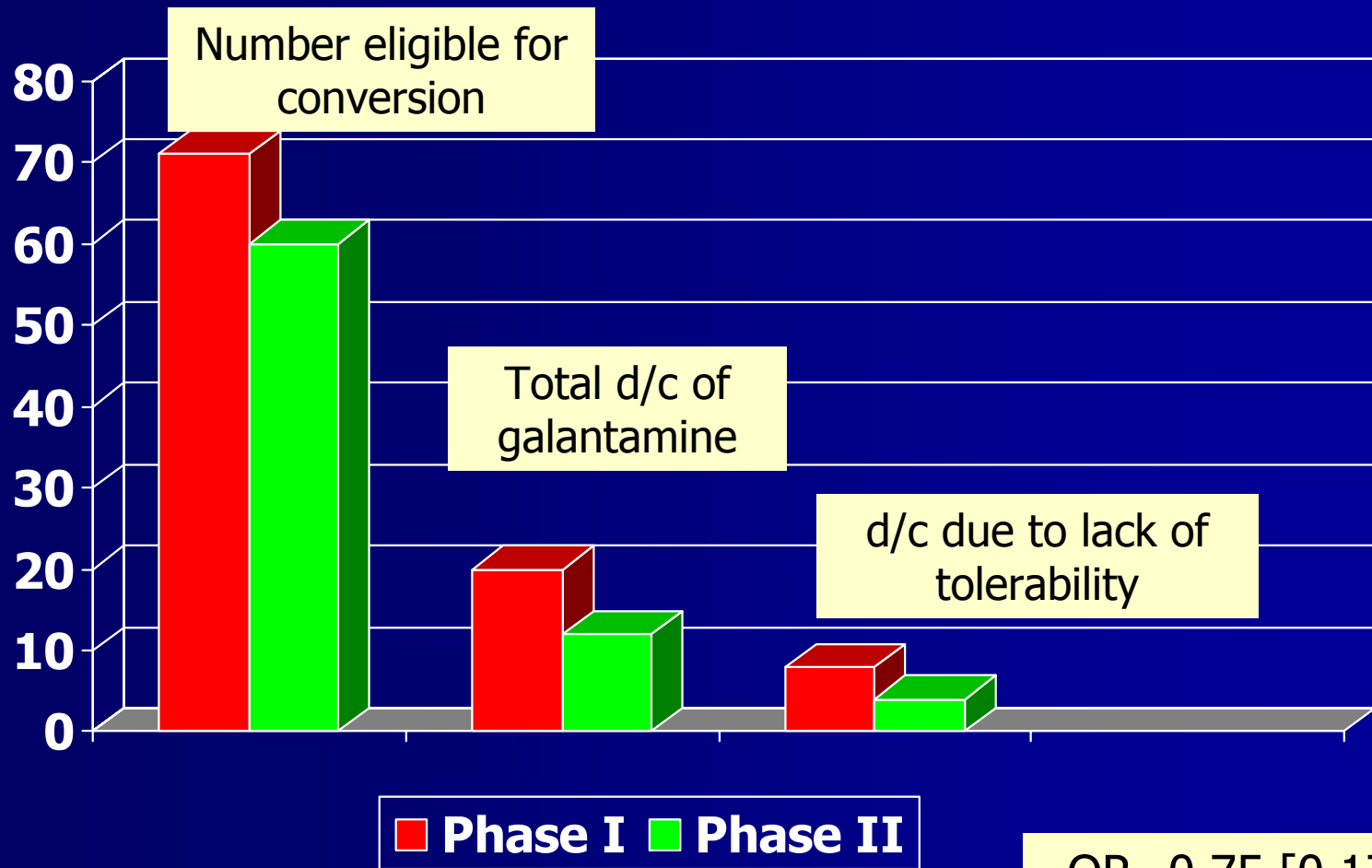
| | Phase I (n=68) | Phase II (n=58) |
|---------------------------------|-------------------|--------------------|
| Gender | | |
| Male | 66 (97%) | 58 (100%) |
| Baseline MMSE | 21.57 ± 6.25 | 22.58 ± 5.67 |
| Baseline ADCS-ADL | 46.70 ± 20.56 | 48.78 ± 17.09 |
| Baseline Adverse Effects | | |
| (none - a little) | 61 (95%) | 45 (78%) |
| Nausea | 54 (84%) | 53 (91%) |
| Diarrhea | 59 (92%) | 46 (79%) |
| Appetite | | |

Patient Demographics



- Alzheimer's disease
- Memory loss/mild cognitive impairment
- Dementia NOS
- Vascular
- Presenile/senile
- Organic brain syndrome
- Other

Galantamine Tolerability



OR=0.75 [0.17-3.35]

Results

- Reasons for discontinuation
 - **nausea** (n=6)
 - **diarrhea** (n=5)
 - **loss of appetite** (n=3)
 - mood/personality change (n=2)
 - dizziness (n=1)
 - hallucinations (n=1)
 - increased symptoms associated with GERD (n=1)

Study Limitations

- Small sample size
- Concomitant medications
- Patient population

Conclusion

- Patients previously treated with donepezil tolerated a galantamine titration which was accelerated compared to the regimen suggested in the galantamine product information

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References

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