Reviewer’s report

Title: Response to cholinesterase inhibitors might affect life-span in Alzheimer’s disease

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Reviewer: Ezio Giacobini

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TITLE OK but , why not , ...... inhibitors affect .....

ABSTRACT
Heterogeneous , differential response, please specify
Conclusion : was tolerance the only criterion for dosage ?

INTRODUCTION
Problem of mortality in AD, highly depending on comorbidity, difficult to point out a direct relationship with the disease, AD patients live longer and longer with better care, not rare are 15—20 yrs after diagnosis, the same in Parkinson.

Level of response is heterogeneous, please specify

METHODS
Conflicting results about treatment-mortality relation : discuss in Discussion

Was the clinical diagnosis confirmed with autopsy ? very important point related to comorbidity

Reason for using only the first 6 mo while treatment continued up to 3 years , treatment duration could be more relevant than treatment dosage.

Why to use only MMSE while ADAS-Cog data were available , both measures would have been better to evaluate relation to treatment effect.

Were all 14 sites standardized to diagnosis and treatment ?

63 % patients showed stabilization/no-change or improvement : how many were stable and how many were improved ? again ADAS-Cog is important.

DISCUSSION
Milder disease severity shows more favourable response : some studies showed the opposite with best results in more severe patients . Discuss,

Possible relation to treatment duration. Discuss

Comorbidity and autopsy results : Discuss
Other factors to be considered.

Anti-inflammatory effect of ChEI

Immunonogical factors

Quality of life and caregiver burden to be considered

Conclusions: consistent with findings