

tolerability of subcutaneous etanercept in patients with Alzheimer disease (AD) dementia. Although it was not their primary outcome, the authors hypothesized that etanercept could decrease systemic inflammation and result in cognitive benefits.

Butchart et al. previously observed that baseline increased inflammatory marker levels were associated with more rapid decline in cognitive functions in patients with AD dementia.^{2,3} However, the levels of inflammatory markers in the current study are relatively low in comparison with those reported in their previous studies. Tumor necrosis factor range was 1.8–3.2 pg/mL in the current study, while it was >3.27 pg/mL in the highest 2 quartiles in the previous study.

In addition, interleukin (IL)–6 range was 0.5–1.5 pg/mL in the current study, while it was >2.8 pg/mL in the group with higher IL-6 in the previous study. Absence of low-grade systemic inflammation in the baseline visit may have attenuated a potentially beneficial effect of etanercept on cognitive functions in this study. Finally, the C-reactive protein (CRP) levels may be incorrect: they seem very high at 1.8 mg/mL and may actually have been 1.8 µg/mL. Studying subjects with higher baseline levels of

inflammatory markers in further studies might provide valuable information.

Author Response: Clive Holmes, Southampton, UK:

We thank Tufan et al. for their comments. The levels of the proinflammatory cytokines are lower than in our previously published observational cohort, but not substantially. The levels may just reflect variability between subjects or different plate batches with mesoscale discovery assays. However, we would agree that subjects with higher levels of inflammation may have greater benefit and this is worthy of further investigation. Tufan et al. are also correct about the CRP levels; we should have reported them as µg/mL, not mg/mL.

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1. Butchart J, Brook L, Hopkins V, et al. Etanercept in Alzheimer disease: a randomized, placebo-controlled, double-blind, phase 2 trial. *Neurology* 2015;84:2161–2168.
2. Holmes C, Cunningham C, Zotova E, et al. Systemic inflammation and disease progression in Alzheimer disease. *Neurology* 2009;73:768–774.
3. Holmes C, Cunningham C, Zotova E, Culliford D, Perry VH. Proinflammatory cytokines, sickness behavior, and Alzheimer disease. *Neurology* 2011;77:212–218.

CORRECTION

Etanercept in Alzheimer disease: A randomized, placebo-controlled, double-blind, phase 2 trial

In the article “Etanercept in Alzheimer disease: A randomized, placebo-controlled, double-blind, phase 2 trial” by J. Butchart et al. (*Neurology*[®] 2015;84:2161–2168), there is an error in the unit of measure used to report the CRP levels. They should have been reported as µg/mL rather than mg/mL. The authors regret the error.

Author disclosures are available upon request (journal@neurology.org).

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Etanercept in Alzheimer disease: A randomized, placebo-controlled, double-blind, phase 2 trial

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