Nonmelanoma skin cancer is associated with reduced Alzheimer disease risk
Friedrich P. Thinnes, Göttingen, Germany: I propose a biologically based hypothesis for the association between skin cancer and reduced Alzheimer disease (AD) risk.1 Amyloid Aβ peptides, cut from the amyloid precursor protein of neurons, are assumed to induce brain-wide neuronal apoptosis via opening plasma lemma-standing type 1 voltage-dependent anion channels (VDAC). This process results in AD whenever critical brain regions are affected.2–4 Either reaction partner carries one or several GxxxG motifs. Furthermore, data indicate that amyloid Aβ peptides can be extruded from the brain by ABC transporters at the blood–brain barrier and cancerous transformations accompany changes in the expression level or the functionality of multidrug resistance modulators that then disturb chemotherapy.5 However, enhanced extrusion of apoptogenic amyloid A by raised ABC transporter activities of cancer survivors might diminish or even abolish intrabrain apoptotic effect. These findings, along with other data,6 may explain why cancer survivors have a lower risk of AD. Finally, the VDAC/amyloid interaction model of AD pathogenesis could explain the reverse relationship of AD and cancer.5

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Treatment with statins and ischemic stroke severity: Does the dose matter?
Joshua Willey, New York: Martínez-Sánchez et al. addressed the issue of nonrandomization of trial participants taking statins before stroke (confounding by indication), using propensity scores.1 This statistical method may not fully account for prestroke imbalances, which may affect the probability that a patient would be prescribed a statin as an outpatient. For example, older patients with atrial fibrillation (AF) who are likely to have larger strokes may be less likely to be prescribed statins (table 1).1 Comparing tables 1 and 2, what accounts for the difference in the proportion of patients with AF and those with cardioembolic strokes? What would occur if AF, or cardioembolic vs all others, was included in the models from table 3? In those models, all stroke subtypes are included but with such small numbers that a model fit may be problematic. Until a clinical trial is completed with high doses acutely administered, we caution against high doses being administered to all stroke types. The data support not withholding statins,2 but at least one study raised the possibility of no benefit from statins in the acute setting with a trend to worse outcomes.3

Author Response: Patricia Martínez-Sánchez, Blanca Fuentes, Elena Díaz-Domínguez, Marta Martínez-Martínez, Exuperio Díez-Tejedor, Madrid: We thank Dr. Willey for his comments on our
Nonmelanoma skin cancer is associated with reduced Alzheimer disease risk
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