Retrospective Analyses of Dementia Outcomes in Patients Prescribed Immunosuppressants

Jacqueline Silva,1 Daniel Jupiter,2 and Giulio Taglialatela2

1Univ of Texas Medical Branch at Galveston; and 2University of Texas Medical Branch

Background: The prevalence of dementia is approximately 11% in patients aged 65 and over in the US. Evidence suggests that patients treated with immunosuppressive calcineurin inhibitors (CNI) have a lower prevalence of dementia compared to the general population. Whether the observed effects are due to general immunosuppression or specifically to calcineurin inhibition remains unresolved. In this project we use electronic medical records (EMR) obtained from the TriNetX database to test the hypothesis that patients prescribed the CNI immunosuppressant tacrolimus have a lower prevalence of dementia relative to patients prescribed the non-CNI immunosuppressant sirolimus.

Methods: EMRs of patients prescribed tacrolimus or sirolimus were downloaded from the TriNetX Diamond Network, a longitudinal dataset of linked primary care, medical, and pharmacy claims data for over 200 million patients. Patients aged 65 and over who were prescribed the drug of interest for at least one year were analyzed. Patients prescribed both drugs or who were diagnosed with dementia before first recorded drug prescription were excluded from analysis. Patients prescribed tacrolimus were propensity-score matched, by demographics and several dementia risk factors, to those prescribed sirolimus, in a one-to-one ratio. We then retrospectively examined dementia outcomes using bivariate, survival, and competing risk analyses. All analyses were conducted using R version 4.2.0.

Results: Of the 2950 patients in each cohort, 190 (6.4%) prescribed tacrolimus and 202 (6.9%) prescribed sirolimus later developed dementia. Survival and competing risk analyses revealed no significant difference in dementia prevalence between cohorts. However, patients prescribed sirolimus were more likely to experience death relative to patients prescribed tacrolimus (HR = 1.37, p < 0.001).

Conclusion: Our results do not support the hypothesis that patients prescribed tacrolimus have a lower prevalence of dementia relative to patients prescribed sirolimus. Nevertheless, both cohorts have a reduced prevalence of dementia compared to all patients aged 65 and over in the US. We suspect that the decreased prevalence of dementia can be attributed to an alternative converging impact of the diverse mechanisms of action of the two drugs rather than to general immunosuppression. However, the increased risk of death in patients prescribed sirolimus relative to tacrolimus may obscure result interpretation since dead patients are unable to develop dementia. While not significant, these results showcase the importance of presenting the null hypothesis to inform future studies and give mechanistic insight into potential treatments for dementia.

Support/Funding Information: NIH/NIA grant R01AG060718 to GT