OBJECTIVES

It is widely believed that inflammation contributes to the pathogenesis of Alzheimer’s Disease (AD). More recently, the immunosuppressant drug etanercept has been implicated in reducing the risk of AD. Confirmatory research is warranted to determine if it and its anti-TNF-α drug class has in preventing AD, which is the 6th leading cause of death in the US and its incidence continues to rise with an increasing aging population. Therefore, TNF-α inhibitors are surmised to be of potential benefit for preventing AD and are further explored in retrospective study.

METHODS

Patients were identified as either receiving an anti-TNF-α drug (etanercept, adalimumab, certolizumab, infliximab, or golimumab) or anti-TNF-α naïve receiving methotrexate (MTX) as the control arm. Patient cohorts were generated in both an electronic medical records (EMR) research network of 366 patient lives and a 2,053 patient network of linked primary care data with medical and pharmacy claims. Neither cohort had AD (ICD-10: G30) prior to the anytime outcome window. The risk of AD from 1 year after first exposure to either anti-TNF-α or MTX was analyzed using measures of association and survival analyses conducted via Kaplan-Meier estimator. Both sets of cohort comparisons were also run with propensity score matching (PSM) to control for demographic, comorbidity, medication, and diagnostic procedure confounders. (Table 11)

RESULTS

There was significant AD prevention with anti-TNF-α treatment compared to MTX found in both EMR (RR 1.824, p = <0.0001) and claims data networks (RR 1.376, p = <0.0001) before PSM. (Table 2) Significant results were also yielded in EMR (RR 1.310, p = <0.0001) and claims data networks (RR 1.501, p = <0.0001) with PSM applied. (Table 2) The time to AD outcome was measured up to 5,500 days in the EMR cohort with survival probability 98.577% for anti-TNF-α and 97.095% for MTX (p = <0.0001). In the claims cohorts, survival probability was 97.214% for anti-TNF-α and 94.640% for MTX (p = <0.0001). In those cohorts, survival findings (p = <0.0001) were seen in both the EMR and claims comparisons that used PSM. (Figures 1-4)

CONCLUSIONS

This study provides RWD-based evidence that points to anti-TNF-α therapies as a beneficial treatment in the prevention of AD. These findings are validated in two distinct types of data, EMR and claims, and significance is still evident with PSM applied to both analyses. Further research is warranted to investigate these results in even larger cohorts and to monitor the AD outcome to be monitored in a longer outcome window. Additionally, the effect of TNF-α inhibitors should be explored in other inflammation-related CVD diseases such as multiple sclerosis and the broad “umbrella” diagnosis of dementia in which AD falls within.

REFERENCES

1. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6214864/

Table 1. Baseline cohort characteristics

Table 2. Cohort comparisons before / after PSM matching

Figure 1. EMR cohorts Kaplan-Meier analysis before PSM

Figure 2. EMR cohorts Kaplan-Meier analysis after PSM

Figure 3. Claims cohorts Kaplan-Meier analysis before PSM

Figure 4. Claims cohorts Kaplan-Meier analysis after PSM