ORAL PRESENTATIONS

[ID-O#121] Characterization of risk of torsade de pointes with cholinesterase inhibitors and memantine: A real-world data analysis

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Background and aims: As per WHO estimates, dementia affects more than 55 million people worldwide, with Alzheimer's disease (AD) accounting for 60-70% of these cases. The prevalence is projected to reach 78 million in the next 6 years and 139 million by 2050, driven largely by aging populations in low and middle-income countries [1]. Cholinesterase inhibitors and memantine modestly improve cognition in Alzheimer's disease cases providing symptomatic relief, however, their impact on disease progression remains limited and varies among individuals. During April to June 2023, FDA identified potential signals of Torsade de pointes with cholinesterase inhibitors based on analysis of Adverse Event Reporting System [FAERS] database. The current study was conducted to analyse this relationship and to perform disproportionality analysis of four drugs- donepezil, rivastigmine, galantamine and memantine currently approved for AD patients.

Methods: Adverse event (AE) reports in the FAERS database were utilized commencing from the dates of regulatory approval of the these agents (donepezil- 1996, galantamine- 2001, rivastigmine-2000 and memantine-2003) [2]. Disproportionality analysis was carried out using OpenVigil 2.1, a validated tool for extracting, filtering, cleaning, mining and analysing AE data. Reporting odds ratio (ROR) and Proportional reporting ratio (PRR) with 95% CI were calculated and the event was labelled as significant if the ROR value was >2; lower limit of 95%CI>1; and number of cases (N) reported were at least 3. MedDRA-Medical Dictionary for Regulatory Activities preferred term (PT) - torsade de pointes was used for this analysis.

Results: A total of 90 AEs of interest were detected for donepezil against 4608 adverse events reports. For galantamine there were two AEs of interest while for rivastigmine and memantine, there were 4 and 3 AEs respectively. The ROR (95% CI) values for these drugs were 44.02 (35.67 – 54.32), 2.73 (0.68-10.95), 1.02 (0.38-2.72) and 1.32 (0.43 – 4.09) for donepezil, galantamine, rivastigmine and memantine respectively. For the four AD drugs, chi-squared values (with Yates' correction) were 3609.61, 0.81, 0.04 and 0.02 respectively.

Conclusion: Based on disproportionality analyses of real world reported data, this study demonstrates signals of torsade de pointes for donepezil. It is essential for prescribers to remain vigilant about this risk and to be mindful of potential adverse drug interactions. References: