UNIVERSITY OF COPENHAGEN

PHARMACOVIGILANCE RESEARCH CENTER

Main supervisor.

Assist. Prof. Maurizio Sessa, MPharm, PhD.

Topic.

Pharmacovigilance.

Title of the project.

New insight on the safety of galcanezumab and fremenezumab: an analysis of spontaneous reports of adverse events recorded in the U.S. Food and Drug Administration Adverse Event Reporting System database.

Project description.

Migraine is a common, neurological disorder that affects approximately 12% of the adult population around the world. Patients having this disease require drug-based treatments to prevent and abort migraine attacks. For patients with the inability to tolerate the conventional preventive therapies for migraine and for those reaching inadequate control of the disease, the American Headache Society recommends starting treatment with monoclonal antibodies to calcitonin gene-related peptide (CGRP) or its receptor. CGRP is a peptide released from meningeal and perivascular nerve fibers after trigeminal nerve activation that plays a pivotal role in the pathophysiology of migraine. It contributes to the dilation of vascular beds, neurogenic inflammation, and peripheral sensitization of nociceptive afferents, thus modulating pain signals to the brainstem. Currently, galcanezumab and fremenezumab are two approved monoclonal antibody antagonizing the effects mediated by CGRP on the CGRP receptor for which there is no available study describing their safety profile using adverse events reported in post-marketing. Open-access data on a case-level of adverse events reporting galcanezumab or fremenezumab as suspected or concomitant drug can be found in the Food and Drug Administration (FDA) Adverse Event Reporting System (FAERS). FAERS is a database that stores adverse events reported to the FDA from 1969 onwards that have been developed to supports the post-marketing safety surveillance for all approved drugs and therapeutic biologic products, integrating the safety information that emerged in the drug development process. While spontaneous reports of adverse events have limitations, such as the potential for duplication of cases, no certainty regarding the causal relationship between drugs and adverse events, and being dependent upon spontaneous or voluntary events, it is a valuable data source for assessing the frequency of adverse events reported in post-marketing and generate signals on new potential drug safety problems. In this project, you will screen FAERS for post-marketing reports of adverse events reporting galcanezumab or fremenezumab as a suspected drug from the date of drug approval to provide descriptive analyses of the frequency, severity, and outcomes of adverse events and a case series of fatal cases. Additionally, we aimed at proving an overview of the top 10 reported adverse events by the top-10 system organ classes, a list of adverse events not reported in the summary of product characteristics (SmPC), and a description of adverse events commonly co-reported. Finally, for adverse events not reported in the SmPC, you will perform a disproportionality analysis in comparison with sumatriptan or erenumab, two drugs used for migraine.

Acquired skills: statistical programming in R and SAS; data management; causality assessment; scientific writing.

References

1) Edvinsson, L., Haanes, K.A., Warfvinge, K. et al. CGRP as the target of new migraine therapies — successful translation from bench to clinic. Nat Rev Neurol 14, 338–350 (2018). Nature Reviews Neurology

2) Durham PL, Vause CV. Calcitonin gene-related peptide (CGRP) receptor antagonists in the treatment of migraine. CNS Drugs. 2010;24(7):539-548. doi:10.2165/11534920-000000000-00000