

SFDA SAFETY SIGNAL

“A signal is defined by the SFDA as reported information on a possible causal relationship between an adverse event and a drug, the relationship being unknown or incompletely documented previously. Usually more than a single report is required to generate a signal, depending upon the seriousness of the event and the quality of the information. A signal is a hypothesis together with data and arguments and it is important to note that a signal is not only uncertain but also preliminary in nature”

10-09-2024

Saudi Food and Drug Authority (SFDA) – Safety Signal of Venetoclax and the Risk of Progressive multifocal leukoencephalopathy

*The Saudi Food and Drug Authority (SFDA) recommends all health care professionals to be aware of the safety signal of **Progressive multifocal leukoencephalopathy** associated with the use of **Venetoclax**. The signal has been originated as a result of routine pharmacovigilance monitoring activities.*

Introduction

Venetoclax is a selective and orally bioavailable small-molecule inhibitor of BCL-2, an anti-apoptotic protein. It is indicated for the treatment of adult patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL).^[1] Progressive multifocal leukoencephalopathy (PML) is a disease of the white matter of the brain, caused by a virus infection (polyomavirus JC) that targets cells that make myelin. Polyomavirus JC (often called JC virus) is carried by a majority of people and is harmless except among those with lowered immune defenses.^[2] The aim of this review is to evaluate the risk of Progressive multifocal leukoencephalopathy associated with the use of Venetoclax and to suggest regulatory recommendations if required.

Methodology

Signal Detection team at SFDA performed a signal review using National Pharmacovigilance Center (NPC) database, and World Health Organization (WHO) database, VigiBase, with literature screening to retrieve all related information to assess the causality between Progressive multifocal leukoencephalopathy and Venetoclax use. The search conducted on June 2024.

Results

Case Review: Signal detection team at SFDA have searched Saudi national database and WHO database to find individual case safety reports (ICSRs). The WHO database resulted in 21 global case-reports while no local cases found. The authors used signal detection tool (Vigilyze) to retrieve all reported global cases.^[3] Authors also applied WHO-UMC causality assessment criteria on the extracted ICSR. ^[4] Among them, 8 cases were probably and possibly linked to Venetoclax, and 9 cases assessed as not assessable due to lack of valuable information, while the remaining 4 cases assessed as unlikely.

Datamining: The disproportionality of the observed and the expected reporting rate for drug/adverse drug reaction pair is estimated using information component (IC), a tool developed by WHO-UMC to measure the reporting ratio. Positive IC reflects higher statistical association while negative values indicates less statistical association. The IC result is (2.1) for this drug/ADR combination which reflects positive statistical association. [4]

Conclusion

The weighted cumulative evidence identified from assessed cases and disproportionality analysis are suggestive for causal association between Venetoclax and Progressive multifocal leukoencephalopathy. Health care professionals and health regulators must be aware of the potential risk in drug recipients.

Report Adverse Drug Events (ADRs) to the SFDA

The SFDA urges both healthcare professionals and patients to continue reporting adverse drug reactions (ADRs) resulted from using any medications to the SFDA either online, by regular mail or by fax, using the following contact information:

National Pharmacovigilance Center (NPC)
Saudi Food and Drug Authority-Drug sector
4904 northern ring branch rd
Hittin District
Riyadh 13513 – 7148
Kingdom of Saudi Arabia
Toll free number: 19999
Email: NPC.Drug@sFDA.gov.sa

References:

- 1- National Institutes of Health. (n.d.). DailyMed - venclexta- Venetoclax kit venclexta- Venetoclax tablet, film coated. U.S. National Library of Medicine. <https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=b118a40d-6b56-cee3-10f6-ded821a97018&audience=consumer> [Accessed: 27/06/2024].
- 2- National Institute of Neurological Disorders and Stroke (2024). Progressive Multifocal Leukoencephalopathy. Available at: [https://www.ninds.nih.gov/health-information/disorders/progressive-multifocal-leukoencephalopathy#:~:text=Progressive%20multifocal%20leukoencephalopathy%20\(PML\)%20is.](https://www.ninds.nih.gov/health-information/disorders/progressive-multifocal-leukoencephalopathy#:~:text=Progressive%20multifocal%20leukoencephalopathy%20(PML)%20is.) [Accessed: 27/06/2024].
- 3- Vigilyze.who-umc.org. 2024. [online] Available at: <https://vigilyze.who-umc.org/> [Accessed: 27/06/2024].
- 4- World Health Organization WHO (2013). WHO-UMC system for standardised case causality assessment. Available at <https://www.who.int/publications/m/item/WHO-causality-assessment> [Accessed: 28/06/2024].