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"

21-11-2023

Saudi Food and Drug Authority (SFDA) – Safety Signal of Encorafenib and the Risk of Tumour lysis syndrome

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

Introduction

Encorafenib is indicated for BRAF V600E or V600K Mutation-Positive Unresectable or Metastatic Melanoma, and for BRAF V600E Mutation-Positive Metastatic Colorectal Cancer (CRC). Encorafenib is a kinase inhibitor that targets BRAF V600E, as well as wild-type BRAF and CRAF in in vitro cell-free assays with IC50 values of 0.35, 0.47, and 0.3 nM, respectively. [1] Tumor lysis syndrome is the most common oncologic emergency.is a condition that occurs when a large number of cancer cells die within a short period, releasing their contents in to the blood.When cancer cells break down quickly in the body, levels of uric acid, potassium, and phosphorus rise faster than the kidneys can remove them. This causes TLS. [2] The aim of this review is to evaluate the risk of Tumour lysis syndrome associated with the use of Encorafenib 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 Tumour lysis syndrome and Encorafenib use. The search conducted on August 2023.

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 14 global case-reports. [3] The authors applied WHO-UMC causality assessment criteria on the cases, which resulted in some of them are linked to Encorafenib (1 certain + 2 probable + 1 possible + 10 not assessable = 14 ICSRs). [4]

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, considering the null value equal to zero. The results of (IC= 3.6) revealed a strong positive statistical association for the drug/ADR combination. [3]

Literature: On august 27th 2023, the author searched for eligible publications. As a result one published case report found supportive for this signal. [5]

Conclusion

The weighted cumulative evidence identified from assessed cases, literature and data mining are sufficient to suggest causal association between Encorafenib and Tumour lysis syndrome. 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- Dailymed.nlm.nih.gov. (n.d.). DailyMed - BRAFTOVI- encorafenib capsule. [online] Available at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=235dfc38-0f0b-4037-b501-7a9f4294740c [Accessed 23 Aug. 2023].
2- Gupta, A. and Moore, J.A. (2018). Tumor Lysis Syndrome. JAMA Oncology, 4(6), p.895. doi:https://doi.org/10.1001/jamaoncol.2018.0613.
3- Vigilyze.who-umc.org. 2023. [online] Available at: https://vigilyze.who-umc.org/ [Accessed 23/08/2023].
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 23/08/2023].
5- Byron, Y., Nott, L. and Shackleton, M. (2020) 'Case report: Acute tumour lysis syndrome following encorafenib and binimetinib for v600e metastatic melanoma with large intra-abdominal mass', Melanoma Research, 30(6), pp. 625–627. doi:10.1097/cmr.0000000000000696.