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"

25-03-2024

Saudi Food and Drug Authority (SFDA) – Safety Signal of Capecitabine and the Risk of Metabolic acidosis

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

Introduction

Capecitabine is an orally administered fluoropyrimidine carbamate used for the treatment of paclitaxel- or anthracycline-refractory breast cancer. [1] Metabolic Acidosis is the presence of an acid–base imbalance associated with a plasma bicarbonate concentration below 20 mmol/L. [2] The aim of this review is to evaluate the risk of Metabolic acidosis associated with the use of Capecitabine 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 Metabolic acidosis and Capecitabine use. The search conducted on February 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 73 global case-reports while only one local case found. The authors used signal detection tool (Vigilyze) to retrieve all reported global cases. [3] Authors also applied WHO-UMC causality assessment criteria on ICSRs with completeness score 0.7 and above (n=11). [4] Among them, 8 cases of Metabolic acidosis were either probably or possibly linked to Capecitabine, one case assessed as unlikely and the last two cases were not assessable due to lack of important information.

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 (1.0) for this drug/ADR combination which reflects positive statistical association. [4]

Literature: The signal team searched the literature to find related publications linking this ADR to Capecitabine. The search showed one published case-reports of secondary metabolic acidosis following the use of capecitabine, oxaliplatin, and cetuximab. [5]

Conclusion

The weighted cumulative evidence identified from assessed cases, disproportionality analysis, and literature are sufficient to suggest causal association between Capecitabine and Metabolic acidosis. 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- Dooley M, Goa KL. Capecitabine. Drugs. 1999 Jul;58(1):69-76; discussion 77-8. doi: 10.2165/00003495-199958010-00006. PMID: 10439930. [Accessed: 13/02/2024].

2- Jung, B., Martinez, M., Claessens, Y. E., Darmon, M., Klouche, K., Lautrette, A., Levraut, J., Maury, E., Oberlin, M., Terzi, N., Viglino, D., Yordanov, Y., Claret, P. G., Bigé, N., Société de Réanimation de Langue Française (SRLF), & Société Française de Médecine d'Urgence (SFMU) (2019). Diagnosis and management of metabolic acidosis: guidelines from a French expert panel. Annals of intensive care, 9(1), 92. https://doi.org/10.1186/s13613-019-0563-2 [Accessed: 13/02/2024].

3- Vigilyze.who-umc.org. 2024. [online] Available at: https://vigilyze.who-umc.org/ [Accessed: 14/02/2024].

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: 14/02/2024].

5- Sonnenblick, A., & Meirovitz, A. (2010). Renal tubular acidosis secondary to capecitabine, oxaliplatin, and cetuximab treatment in a patient with metastatic colon carcinoma: a case report and review of the literature. International journal of clinical oncology, 15, 420-422.