

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”

09-08-2022

Saudi Food and Drug Authority (SFDA) – Safety Signal of Everolimus and Risk of Osteonecrosis of Jaw

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

Introduction

Everolimus is an antineoplastic agent. It is a selective mTOR (mammalian target of rapamycin) inhibitor. mTOR is a key serine-threonine kinase, the activity of which is known to be upregulated in a number of human cancers. ^[1] Osteonecrosis of the jaw is a severe bone disease that occurs when there is a loss of blood to the bone. The primary symptom of osteonecrosis of the jaw (ONJ) is exposure of the bone through the gums that doesn't heal for several weeks. ^[2]

Methodology

Signal Detection team at the National Pharmacovigilance Center (NPC) of Saudi Food and Drug Authority (SFDA) performed a comprehensive signal review using its national database as well as the World Health Organization (WHO) database (VigiBase), to retrieve related information for assessing the causality between Everolimus and the risk of osteonecrosis of the jaw. ^[3] WHO-Uppsala Monitoring Centre (UMC) criteria have been used as standard for assessing the causality of the reported cases. ^[4]

Results

Case Review: The number of resulted cases for the combined drug/adverse drug reaction is 129 global Individualized Case Safety Reports (ICSRs) as of June 2022. Cases with completeness score >0.8 were extracted and assessed (n= 26). ^[3] The causality assessment resulted in one probable case, eleven possible cases and five unlikely cases. Nine cases were unassessable.

Data Mining: 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 result of (IC= 2) revealed a positive statistical association for the drug/ADR combination, which means “osteonecrosis

of the jaw” with the use of “Everolimus” have been observed more than expected when compared to other medications available in WHO database. [3]

Literature: Upon conducting a literature search, three case reports were found of jaw osteonecrosis of after receiving Everolimus. [5] [6] [7]

Conclusion

The weighted cumulative evidences identified from causality assessment of the reported cases, and literature are sufficient to support a causal association between Everolimus and the risk of osteonecrosis of the jaw. Health regulators and health care professionals must be aware of this potential risk and it is advisable to monitor any signs or symptoms in treated patients.

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@sfd.gov.sa

References:

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2. Gotoapro.org. 2022. Osteonecrosis of the Jaw | American College of Prosthodontists. [online] Available at: <<https://www.gotoapro.org/symptoms/osteonecrosis-of-the-jaw/>> [Accessed 6/22/2022].
3. Vigilyze.who-umc.org. 2021. [online] Available at: <<https://vigilyze.who-umc.org/>> [Accessed 6/22/2022].
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5. Kim, D., Jung, Y., Park, H. and Jung, H., 2013. Osteonecrosis of the jaw related to everolimus: a case report. British Journal of Oral and Maxillofacial Surgery, 51(8), pp.e302-e304.
6. Yamamoto, D., Tsubota, Y., Utsunomiya, T., Sueoka, N., Ueda, A., Endo, K., Yoshikawa, K. and Kon, M., 2016. Osteonecrosis of the jaw associated with everolimus: A case report. Molecular and Clinical Oncology, 6(2), pp.255-257.
7. Akkach, S., Shukla, L. and Morgan, D., 2019. Everolimus-induced osteonecrosis of the jaw in the absence of bisphosphonates: a case report. British Journal of Oral and Maxillofacial Surgery, 57(7), pp.688-690.