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"

9-8-2021

Saudi Food and Drug Authority (SFDA) – Safety Signal of Atezolizumab and the Risk of Keratitis

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

Introduction

Atezolizumab is an Fc-engineered, humanised immunoglobulin G1 (IgG1) monoclonal antibody that directly binds to PD-L1 and provides a dual blockade of the PD-1 and B7.1 receptors, releasing PD-L1/PD-1 mediated inhibition of the immune response, including reactivating the antitumour immune response without inducing antibody-dependent cellular cytotoxicity. [1] Keratitis is an inflammation of the cornea, the clear, dome-shaped tissue on the front of your eye that covers the pupil and iris. Keratitis may or may not be associated with an infection. Noninfectious keratitis can be caused by a relatively minor injury, by wearing contact lenses too long or by a foreign body in the eye. Infectious keratitis can be caused by bacteria, viruses, fungi and parasites. [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 Atezolizumab and the risk of keratitis. [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 4 global ICSRs as of June 2021. [3] The reviewers have extracted and assessed the causality for all ICSRs. The causality assessment resulted in one possible cases, and three cases were not assessable.

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. The result of (IC= 1.3) revealed a positive statistical association for the drug/ADR combination, which means "keratitis" with the use of "Atezolizumab" have been observed more than expected when compared to other medications available in WHO database. [3]

Literature: Upon conducting a literature search, only a case report that triggered the signal was found. A 46 years old women who suffered from eye pain, redness, and blurred vision for 7 days. She started Atezolizumab two months ago for metastatic bladder cancer. [5]

Regulatory agencies: Keratitis is mentioned in Health Canada drug monograph in the warning and precautions section. [6]

Conclusion

The weighted cumulative evidences identified from causality assessment of the reported cases, data mining and literature are sufficient to support a causal association between Atezolizumab and the risk of keratitis. 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@sfda.gov.sa

References:

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2. Mayo Clinic. 2021. Keratitis - Symptoms and causes. [online] Available at: <https://www.mayoclinic.org/diseases-conditions/keratitis/symptoms-causes/syc-20374110> [Accessed 5/3/2021]
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4. Uppsala Monitoring Center (UMC) (2021), The use of the WHO-UMC system for standardized case causality assessment; Available at <https://www.who.int/medicines/areas/quality_safety/safety_efficacy/WHOcausality_assessment.pdf?ua=1> [Accessed 5/3/2021].
5. Oh, J., 2020. Autoimmune Keratitis after Atezolizumab Treatment. New England Journal of Medicine, 383(15), pp.1468-1468. Oh, J., 2020. Autoimmune Keratitis after Atezolizumab Treatment. New England Journal of Medicine, 383(15), pp.1468-1468.
6. Rochecanada.com. 2021. [online] Available at: <https://www.rochecanada.com/PMs/Tecentriq/Tecentriq_PM_E.pdf> [Accessed 5/3/2021].