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"

28-03-2022

Saudi Food and Drug Authority (SFDA) – Safety Signal of Olaparib and the Risk of Pneumocystis Jirovecii Pneumonia (PCP)

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

Introduction

Olaparib is a indicated as monotherapy for the treatment of adult patients with deleterious or suspected deleterious germline BRCA-mutated (BRCAm), human epidermal growth factor receptor 2 (HER2)-negative metastatic breast cancer who have previously been treated with chemotherapy in the neoadjuvant, adjuvant or metastatic setting. Olaparib has been shown to inhibit growth of select tumor cell lines by inhibiting poly ADP ribose polymerase (PARP), an enzyme involved in DNA repair [1]. Pneumocystis Jirovecii Pneumonia (formerly as Pneumocystis carinii) is an infection of the lung caused by the fungal organism Pneumocystis jirovecii. Typically, it causes clinical disease in severely immunocompromised patients [2-3]. The aim of this review is to evaluate the risk of PCP associated with the use of Olaparib and to suggest regulatory recommendations if required.

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 Olaparib and the risk of PCP [4]. We used the WHO- Uppsala Monitoring Centre (UMC) criteria as standard for assessing the causality of the reported cases [5].

Results

Case Review: As of December 2021, 4 global Individual case safety reports (ICSRs) for the combined drug/adverse drug reaction were found [4]. One assessable ICSR was supportive of association

and PCP was probably associated with Olaparib. Moreover, the reported case revealed positive dechallenge too [5].

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 results of (IC= 1.1) revealed a positive statistical association for the drug/ADR combination [4].

Literature: A case report of a 77-year-old woman was published in May 2021. The patient had a relapsed ovarian cancer metastasizing to the pancreatic head, para-aortic lymph nodes, liver, and splenic hilum. After receiving six cycles of Docetaxel and Carboplatin therapy, she was prescribed Olaparib as maintenance therapy. Two months after the Olaparib therapy, the patient complained of a fever, fatigue, and appetite loss. She visited Emergency Department, and pneumonia was suspected, for which she received Ceftriaxone, but her symptoms did not improve. Chest computed tomography (CT) revealed bilateral ground-glass opacity (GGO), highlighting the probability of Pneumocystis Jirovecii Pneumonia. She was given Prednisolone and Trimethoprim/Sulfamethoxazole. Following days in respiratory care, Pneumocystis Jirovecii Pneumonia was confirmed by polymerase chain reaction (PCR) of bronchoalveolar lavage fluid sample [6].

Conclusion

The weighted cumulative evidence identified from the reported cases, data mining and literature are sufficient to support a causal association between Olaparib and the risk of PCP. 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:

1. AstraZeneca (2021). Saudi Summary of Product Characteristics (SPC) of Lynparza- Olaparib Available at: https://sdi.sfda.gov.sa
2. Avino, L. J., Naylor, S. M., & Roecker, A. M. (2016). Pneumocystis jirovecii Pneumonia in the Non-HIV-Infected Population. The Annals of pharmacotherapy, 50(8), 673–679. https://doi.org/10.1177/1060028016650107 [Accessed 20 January 2021].
3. The risk of Pneumocystis carinii pneumonia among men infected with human immunodeficiency virus type 1. Multicenter AIDS Cohort Study Group. N Engl J Med. 1990 Jan 18;322(3):161-5

4. Vigilyze.who-umc.org. 2021. [online] Available at: <https://vigilyze.who-umc.org/>
5. 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
6. Himeji, D., Tanaka, G. I., Shiiba, R., Matsumoto, R., Takamura, K., Morishita, H., Taniguchi, S., Moriguchi, S., & Marutsuka, K. (2021). Pneumocystis Pneumonia in a Patient with Ovarian Cancer Receiving Olaparib Therapy: A Case Report. Internal medicine (Tokyo, Japan), 10.2169/internalmedicine.7485-21. Advance online publication. https://doi.org/10.2169/internalmedicine.7485-21