

## 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”*

27-08-2025

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### Saudi Food and Drug Authority (SFDA) – Safety Signal of Tisagenlecleucel and the Risk of Pneumonia

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

#### Introduction

Tisagenlecleucel is a chimeric antigen receptor (CAR) T-cell therapy. This drug is a CD19-directed genetically modified autologous T-cell immunotherapy. Tisagenlecleucel is currently approved in major markets for the treatment of relapsed/refractory (r/r) pediatric and young adult acute lymphoblastic leukemia, r/r diffuse large B-cell lymphoma, and r/r follicular lymphoma. <sup>[1]</sup> Pneumonia is an umbrella term for a group of syndromes caused by a variety of organisms that result in infection of the lung parenchyma. <sup>[2]</sup> The aim of this review is to evaluate the risk of Pneumonia associated with the use of Tisagenlecleucel 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 Pneumonia and Tisagenlecleucel use. The search conducted on June 2025.

#### 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 63 global case-reports while no local cases found. The authors used signal detection tool (Vigilyze) to retrieve global cases. <sup>[3]</sup> Authors also applied WHO-UMC causality assessment criteria on the extracted ICSR with completeness score 0.6 and above (20 cases). <sup>[4]</sup> Among them, five cases were possibly linked to Tisagenlecleucel, two cases assessed as unlikely, while the remaining thirteen cases were unable to be assessed 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 (1.1) for this drug/ADR combination which reflects positive statistical association. <sup>[4]</sup>



**Literature:** The signal team searched the literature to find related publications linking this ADR to Tisagenlecleucel. The search showed two publications describing Pneumonia as adverse reaction following the use of Tisagenlecleucel. <sup>[5, 6]</sup>

### **Conclusion**

The weighted cumulative evidence identified from assessed cases, disproportionality analysis and literature are suggestive for causal association between Tisagenlecleucel and Pneumonia. 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](mailto:NPC.Drug@sfda.gov.sa)

### **References:**

- 1- Awasthi, R., Maier, H. J., Zhang, J., & Lim, S. (2023). Kymriah® (tisagenlecleucel) - An overview of the clinical development journey of the first approved CAR-T therapy. *Human vaccines & immunotherapeutics*, 19(1), 2210046. <https://doi.org/10.1080/21645515.2023.2210046>
- 2- Jain V, Vashisht R, Yilmaz G, et al. Pneumonia Pathology. [Updated 2023 Jul 31]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK526116/>
- 3- Vigilyze.who-umc.org. 2025. [online] Available at: <https://vigilyze.who-umc.org/>
- 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>
- 5- Schuster, S. J., Tam, C. S., Borchmann, P., Worel, N., McGuirk, J. P., Holte, H., ... & Maziarz, R. T. (2021). Long-term clinical outcomes of tisagenlecleucel in patients with relapsed or refractory aggressive B-cell lymphomas (JULIET): a multicentre, open-label, single-arm, phase 2 study. *The Lancet Oncology*, 22(10), 1403-1415.
- 6- Zipper, R., Loeb, D. M., Lee, M. A., Oliver-Krasinski, J., Liszewski, M. C., & Frint, E. (2023). Respiratory Failure Due to Idiopathic Pneumonia Syndrome in a Pediatric Patient After Recipient-derived Allogeneic Chimeric Antigen Receptor T-Cell Therapy. *Journal of Pediatric Hematology/Oncology*, 45(6), e775-e780.