Direct Healthcare Professional Communication (DHPC)

23 July 2024

Carvykti, Kymriah, Yescarta and Tecartus (CD19- or BCMA-directed CAR T-cell therapies): Risk of secondary malignancy of T-cell origin

Dear Healthcare professional,

Johnson & Johnson, Gilead/Kite and Novartis, in agreement with the Saudi Food and Drug Authority (SFDA), would like to inform you of the following:

Summary

- **Secondary malignancies of T-cell origin, including chimeric antigen receptor (CAR)-positive malignancies, have been reported within weeks and up to several years following treatment of haematological malignancies with a BCMA- or CD19-directed CAR T-cell therapy.**
- **Patients should be monitored life-long for secondary malignancies.**

Background on the safety concern

Currently approved CD19- or BCMA-directed CAR-T cell therapies cover a range of indications spanning from B-cell acute leukaemia, specific subtypes of B-cell lymphoma, and multiple myeloma.

Up to April 2024, approximately 42,500 patients have been treated with these medicinal products globally.

The European Medicines Agency (EMA) has evaluated 38 cases of T-cell malignancy that have been reported to occur after treatment with CAR T-cell therapies up to April 2024. These cases related to different types of T-cell lymphoma and T-cell lymphocytic leukaemia and were observed within weeks and up to several years after administration. There have been fatal outcomes.

Among the cases included in this review, further testing regarding the presence of the CAR-construct in the secondary malignancy had been undertaken for less than half of the reported T-cell malignancies. In 7 cases, the CAR-construct was detectable. This suggests that the CAR T-cell therapy was involved in disease development and insertional mutagenesis could have occurred. While other mechanisms may also be possible, further investigation is desirable to better understand and identify underlying mechanisms and contributing factors. Therefore, testing of T-cell malignancy tissue samples from patients is one important step for such investigations.

Since approval, the product information has advised that patients treated with these products may develop secondary malignancies. The product information will be updated to include the new information concerning secondary malignancy of T-cell origin. Patients treated with CAR T-cell products should be monitored life-long for secondary malignancies.

Call for reporting

Please report any suspected adverse reactions associated with the use of CAR T-cell products in accordance with the national requirements via the national spontaneous reporting system, to:

Saudi Food and Drug Authority National Pharmacovigilance Center
Unified Contact Center: 19999
Email: npc.drug@sfda.gov.sa
Or by online: https://ade.sfda.gov.sa

And to the company on:

CAR-T product name	Company name	Patient Safety Department Contact details
KYMRIAH® (tisagenlecleucel)	Novartis	Toll Free Number: 8001240078 Phone: +966112658100 Fax: +966112658107 Email: adverse.events@novartis.com Or by online: https://report.novartis.co
Yescarta (axicabtagene ciloleucel). Tecartus (brexucabtagene autoleucel).	Gilead/Kite	E-mail: Drugsafety.ksa@gilead.com
Carvykti (ciltacabtagene autoleucel)	Johnson & Johnson	Hotline: 00966540015811 Email: GCC-PV2@its.jnj.com

Company contacts point

CAR-T product name	Company name	Patient Safety Department Contact details
KYMRIAH® (tisagenlecleucel)	Novartis	Hajer M. AlSaleh Patient Safety Manager & QPPV Phone (+966) 11 265 8100 Mobile (+966) 553554035 Hager.alsaleh@novartis.com
Yescarta (axicabtagene ciloleucel) Tecartus (brexucabtagene autoleucel)	Gilead/Kite	Mohannad Alghamdi Head of Patient Safety & QPPV Mobile: (+966) 552244297 Mohannad.alghamdi@gilead.com
Carvykti (ciltacabtagene autoleucel)	Johnson & Johnson	Rawan Abuzaid Local Safety Officer & QPPV Phone: (+966) 540 015811 Mobile: (+966) 543938340 rabuzaid@its.jnj.com

Sincerely,

Hajer Alsaleh
Patient Safety Manager/Saudi QPPV of Novartis

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Reason: I am approving this document
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Mohannad Alghamdi
Head of Patient Safety & QPPV of Gilead/Kite

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Rawan Abuzaid
Local Safety Officer & QPPV of Johnson & Johnson

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