16 September 2021
EMA/549742/2021

CHMP endorses review finding no link between viral vector in Zynteglo and blood cancer

On 22 July 2021, EMA's human medicines committee (CHMP) endorsed findings of a review which concluded that there is no evidence Zynteglo causes a blood cancer known as acute myeloid leukaemia (AML).

Zynteglo, a gene therapy for the blood disorder beta thalassaemia, uses a viral vector (or modified virus) to deliver a working gene into the patient's blood cells.

The review considered two cases of AML in patients treated with an investigational medicine, bb1111, in a clinical trial for sickle cell disease. Although there have been no reports of AML with Zynteglo, both medicines use the same viral vector and there was a concern that the vector may be implicated in the development of the cancer (insertional oncogenesis).

The review by EMA's safety committee (PRAC) supported by experts from the Committee for Advanced Therapies (CAT) found that the viral vector was unlikely to be the cause. In one of the patients, the viral vector was not present in the cancer cells, and in the other patient it was present at a site (VAMP4) that does not appear to be involved in cancer development.

After examining all the evidence, it was clear that more plausible explanations for the AML cases included the conditioning treatment the patients received to clear out bone marrow cells and the higher risk of blood cancer in people with sickle cell disease.

Patients having Zynteglo treatment for beta thalassaemia also need conditioning treatment to clear out their bone marrow cells before receiving Zynteglo. Healthcare professionals should therefore explicitly inform patients receiving Zynteglo of the increased risk of blood cancers from medicines used in conditioning treatments.

The CHMP agreed on an update of recommendations for monitoring patients. Healthcare professionals should now check their patients for signs of blood cancers **at least** once a year for 15 years.[1]

The CHMP concluded that the benefits of Zynteglo continue to outweigh its risks. As for all medicines, the EMA will monitor any new data on its safety and update advice for patients and healthcare professionals when necessary.

[1] The previous recommendation was for healthcare professionals to check for signs of cancer once a year.

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Information for patients

- An EMA review has found no evidence that the viral vector in Zynteglo causes a blood cancer known as acute myeloid leukaemia (AML).
- Zyntelgo will continue to be used as before. Your healthcare professional may, however, invite you for cancer screening more frequently than once a year.
- If you have any question about your treatment, speak to your healthcare professional.

Information for healthcare professionals

- EMA's review has concluded that there is no evidence that the viral vector in Zynteglo causes AML.
- Although two patients who received the same viral vector in another medicine had AML, there are more plausible explanations than insertional oncogenesis, including the conditioning treatment the patients received and the higher risk of haematological cancer in people with sickle cell disease.
- Healthcare professionals should explicitly inform patients receiving Zynteglo of the increased risk of blood cancers from medicines used in conditioning treatments.
- Healthcare professionals should continue monitoring patients for cancer. EMA has updated its recommendation for cancer screening, changing the requirement from once a year to **at least** once a year.

More about the medicine

Zynteglo is a one-time treatment for a blood disorder known as beta thalassaemia in patients 12 years and older who require regular blood transfusions.

To make Zynteglo, the stem cells taken from the patient's blood are modified by a virus that carries working copies of the beta-globin gene into the cells. When these modified cells are given back to the patient, they are transported in the bloodstream to the bone marrow where they start to make healthy red blood cells that produce beta-globin. The effects of Zynteglo are expected to last for the patient's lifetime.

Zynteglo was granted conditional marketing authorisation in May 2019. The conditional authorisation means that there is more evidence to come about the medicine, which the company will provide. EMA regularly reviews new information that becomes available.

More about the procedure

The review of Zynteglo was initiated on 18 February, 2021 at the request of the European Commission, under Article 20 of Regulation (EC) No 726/2004.

The review was first carried out by the Pharmacovigilance Risk Assessment Committee (PRAC), the committee responsible for the evaluation of safety issues for human medicines, which worked closely with experts from the Committee for Advanced Therapies (CAT).

The PRAC recommendations were sent to the CAT, which adopted a draft opinion on 16 July 2021 in line with the PRAC recommendations, and subsequently to the Committee for Medicinal Products for Human Use (CHMP), responsible for questions concerning medicines for human use. On 22 July 2021, the CHMP adopted the Agency's final opinion taking into account the draft opinion of the CAT. The CHMP opinion was forwarded to the European Commission, which issued a final legally binding decision applicable in all EU Member States on 16 September 2021.