Drug & Poison Information Center Bulletin
Faculty of Pharmacy - Tanta University

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Inside this issue:

Marburg virus outbreak…..the story behind !

On 13th February, Equatorial Guinea confirmed its first-ever outbreak of Marburg virus disease. Preliminary tests carried out following the deaths of at least nine people in the country's eastern Kie Ntem Province turned out positive on one of the samples for the viral haemorrhagic fever. Equatorial Guinean health authorities sent samples to the Institute Pasteur reference laboratory in Senegal with support from World Health Organization (WHO) to determine the cause of the disease after an alert by a district health official on 7 February. Of the eight samples tested at Institute Pasteur, one turned out positive for the virus. So far nine deaths and 16 suspected cases with symptoms including fever, fatigue, blood-stained vomit, and diarrhea have been reported. Further investigations are ongoing. Advance teams have been deployed in the affected districts to trace contacts, isolate and provide medical care to people showing symptoms of the disease. Efforts are also underway to rapidly mount emergency response, with WHO deploying health emergency experts in epidemiology, case management, infection prevention, laboratory and risk communication to support the national response efforts and secure community collaboration in the outbreak control.

"*Marburg is highly infectious. Thanks to the rapid and decisive action by the Equatorial Guinean authorities in confirming the disease, emergency response can get to full steam quickly so that we save lives and halt the virus as soon as possible,*" said Dr Matshidiso

Overview:

Marburg virus disease (MVD) is a rare but severe hemorrhagic fever which affects both people and non-human primates. MVD is caused by the Marburg virus, a genetically unique zoonotic (or, animal-borne) RNA virus of the filovirus family. The six species of Ebola virus are the only other known members of the filovirus family. The reservoir host of Marburg virus is the African fruit bat, Rousettus aegyptiacus. Fruit bats infected with Marburg virus do not show obvious signs of illness. Primates (including people) can become infected with Marburg virus, and may develop serious disease with high mortality. Further study is needed to determine if other species may also host the virus.

Transmission:

The virus spreads through contact (such as through broken skin or mucous membranes in the eyes, nose, or mouth) with:

- Blood or body fluids (urine, saliva, sweat, feces, vomit, breast milk, amniotic fluid, and semen) of a person who is sick with or died from Marburg virus disease,
- Objects contaminated with body fluids from a person who is sick with or has died from Marburg virus disease (such as clothes, bedding, needles, and medical equipment),
- Semen from a man who recovered from MVD (through oral, vaginal, or anal sex). There is no evidence that Marburg virus can spread through sex or other contact with vaginal fluids from a woman who has had MVD.

Signs and Symptoms:

After an incubation period of **2-21** days, symptom onset is sudden and marked by fever, chills, headache, and myalgia. Around the fifth day after the onset of symptoms, a maculopapular rash, most prominent on the trunk (chest, back, stomach), may occur. Nausea, vomiting, chest pain, a sore throat, abdominal pain, and diarrhea may appear. Symptoms become increasingly severe and can include jaundice, inflammation of the pancreas, severe weight loss, delirium, shock, liver failure, massive hemorrhaging, and multi-organ dysfunction. The case-fatality rate for MVD is between 23-90%.

Risk of Exposure:

People may be at risk of exposure to Marburg virus if they have close contact with:

- African fruit bats (Rousettus aegyptiacus, the reservoir host of Marburg virus), or their urine and/or excretions,
- People sick with Marburg virus disease,
- Non-human primates infected with Marburg virus.

Exposure risk can be higher for those travelers visiting endemic regions in Africa who have contact with fruit bats (Rousettus aegyptiacus), or enter caves or mines inhabited by these bats.

Treatment:

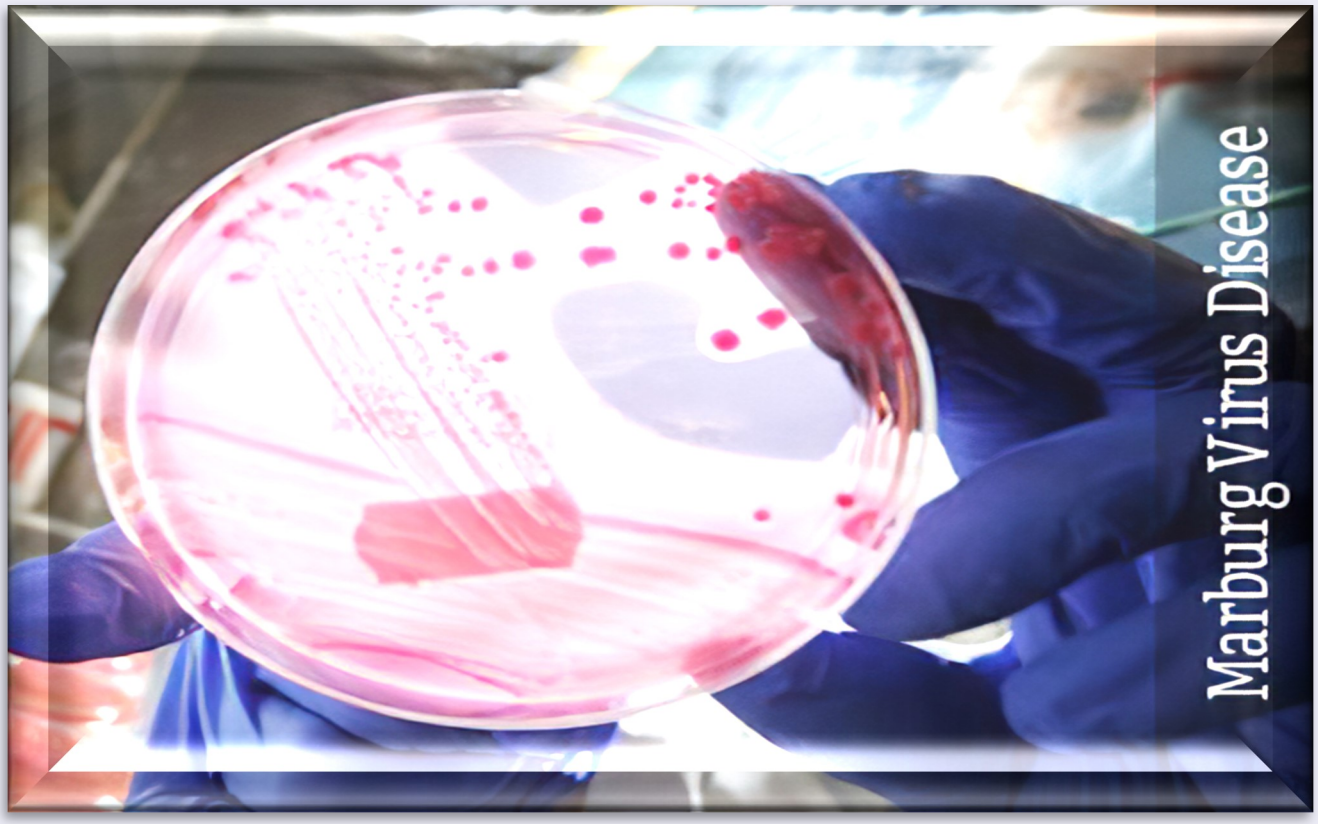
There are no vaccines or antiviral treatments approved to treat the virus. However, supportive care – rehydration with oral or intravenous fluids – and treatment of specific symptoms, improves survival. A range of potential treatments, including blood products, immune therapies and drug therapies, as well as candidate vaccines with phase 1 data are being evaluated.

Prevention:

Measures for prevention of secondary, or person-to-person, transmission are like those used for other hemorrhagic fevers. If a patient is either suspected or confirmed to have Marburg virus disease (MVD), infection prevention and control measures should be used to prevent direct physical contact with the patient. These precautions include wearing protective gowns, gloves, and masks; placing the infected individual in strict isolation; and sterilization or proper disposal of needles, equipment, and patient excretions.

References:

- *Equatorial Guinea confirms first-ever Marburg virus disease outbreak. Available at: https://www.afro.who.int/countries/equatorial-guinea/news/equatorial-guinea-confirms-first-ever-marburg-virus-disease-outbreak. Accessed in February, 2023.*
- *Marburg (Marburg Virus Disease). Available at: https://www.cdc.gov/vhf/marburg/index.html. Accessed in February, 2023.*



By: Marwa Elsayed, PGCPD.

Libmeldy … A £2.8 million gene therapy cures a girl form a rare inherited genetic disease

Last February, a 19-month old English girl diagnosed with Metachromatic Leukodystrophy (MLD), a rare and deadly genetic disease, is cured using a revolutionary gene therapy, and is expected to live a long and normal life. The gene therapy in question, which is called Libmeldy, have been developed by Orchard Therapeutics, with a list price of £2.8 million. The drug was given marketing authorization by European Medicines Agency in 2020.

What about MLD? :

MLD is a rare inherited disorder which belongs to a larger group of inherited lysosomal storage diseases, some of which are progressive and neurodegenerative disorders. It is caused by a mutation in a gene needed to make an enzyme called arylsulfatase A (ARSA), which breaks down substances called sulfatides. As a result, sulfatides build up and damage the nervous system and other organs, causing symptoms such as walking difficulties, gradual mental deterioration and eventual death. Four types of MLD occur with varying ages at onset and courses (ie, late infantile, early juvenile, late juvenile, and adult). Morbidity and mortality rates vary with each form of the disease. In general, young patients have the most rapidly progressive disease, whereas patients with adult onset MLD experience a more chronic and insidious progression of disease.

What is Libmeldy?

Libmeldy (atidarsagene autotemcel) is a gene therapy. The active substance in Libmeldy is stem cells, (CD34+ cells), derived from the patient's own bone marrow or blood, that have been modified to contain a copy of the gene to make ARSA and can divide to produce other sorts of blood cells.

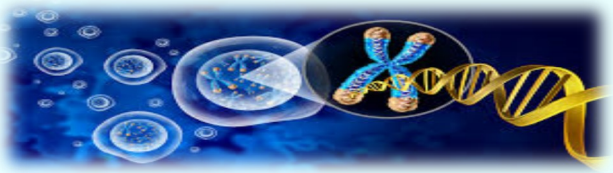
Orchard therapeutics

libmeldy™

Indications:

Libmeldy is indicated for the treatment of metachromatic leukodystrophy (MLD) characterized by biallelic mutations in the arylsulfatase A (ARSA) gene leading to a reduction of the ARSA enzymatic activity:

- In children with late infantile or early juvenile forms, without clinical manifestations of the disease,
- In children with the early juvenile form, with early clinical manifestations of the disease, who still have the ability to walk independently and before the onset of cognitive decline.

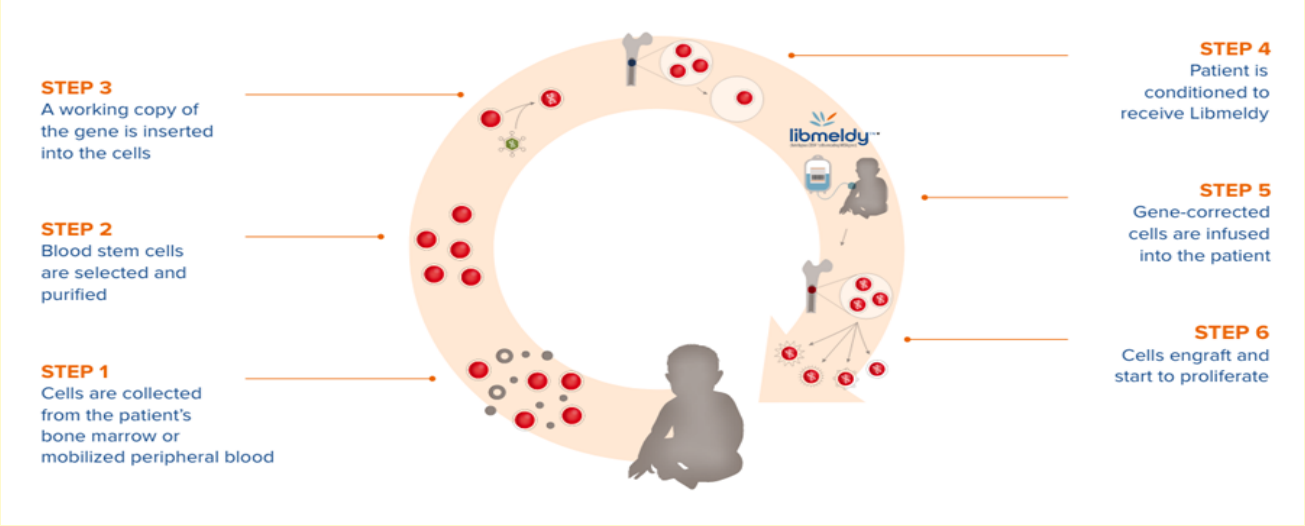


Dosage and Administration

The dose of Libmeldy to be administered is defined based on the patient's weight at the time of infusion. The minimum recommended dose of Libmeldy is 3 × 106 CD34+ cells/kg. In clinical studies, doses up to 30 × 106 CD34+ cells/kg have been administered. Libmeldy is intended for autologous use (i.e. involving one individual as both donor and recipient) and should only be administered once.

Preparation:

To prepare Libmeldy, a sample containing stem cells is collected either from the patient's bone marrow or blood. These are modified to make Libmeldy by including a copy of the gene to make ARSA. Libmeldy can only be given to the patient whose cells were used to make the medicine. It is a single treatment, given as an infusion (drip) into a vein, and the dose depends on the patient's weight. A few days before treatment another medicine, busulfan, is given as a conditioning treatment, to clear out existing bone marrow cells so they can be replaced with the modified cells in Libmeldy. Patients are also given other medicines before treatment to reduce the risk of reactions.



How does Libmeldy work:

To make Libmeldy, the CD34+ cells (cells that can make white blood cells) are extracted from the blood or bone marrow. A gene allowing them to make ARSA is inserted into the CD34+ cells using a type of virus called a lentivirus, which has been altered genetically so that it can carry the ARSA gene into cells and does not cause viral disease in humans. Once given back into the patient's vein, Libmeldy is transported in the bloodstream to the bone marrow where the CD34+ cells start to grow and make normal white blood cells that can produce working ARSA. These white blood cells spread through the body and produce ARSA, helping to break down sulfatides in the surrounding cells, and so controlling symptoms of the disease. The effects are expected to be long-lasting.

Adverse Effects and risks:

The most common side effect with Libmeldy (which may affect more than 1 in 10 people) is development of antibodies to ARSA, although this does not seem to affect how well Libmeldy works. As a result of the conditioning treatment with busulfan, febrile neutropenia, metabolic acidosis, stomatitis, vomiting, hepatomegaly, veno-occlusive liver disease and ovarian failure in girls are also very common.

Libmeldy must not be used in patients who have had previous gene therapy involving blood stem cells, or in those who cannot be given the medicines needed to prepare them for producing or receiving Libmeldy.

References:

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- *Girl with deadly inherited condition is cured with gene therapy on NHS. Available at: https://www.theguardian.com/society/2023/feb/15/girl-with-deadly-inherited-condition-mld-cured-gene-therapy-libmeldy-nhs. Accessed in February, 2023.*

By: Amr Nowier, B.Sc.

Within the framework of supporting and developing student activities and community services, and under the auspices of Prof. Dr. Sahar Muhammad Al-Hajjar, Acting Dean of the College and Vice Dean for Community Service and Environmental Development, the Drug and Poison Information Center of the College celebrated honoring the winning students in the awareness competition on antibiotic resistance, which included choosing the best awareness video to be presented as a meaningful awareness message..

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Vision

The vision of Tanta University DPIC is to improve national healthcare service through provision of evidence-based, unbiased, patient oriented drug information services & adverse drug reporting system.

Mission

* Responding to drug inquiries related to the use of the drug and providing the health care professionals and patients with drug information related to the patient's care to achieve the optimal use of the drug in addition to the provision of other toxicological managing information.
* Educational activities to support the rational optimal use of drugs as well, supporting research activities.
* Continuous medical education and training courses in various fields of pharmacy for students, undergraduates, postgraduate students, and researchers.
* Issuing a Drug Information Bulletin periodically to take a look at medical & pharmaceutical news.
* Supporting the National Pharmaceutical Vigilance Program by following up and monitoring side effects and problems related to use of pharmaceutical preparations within regional hospitals.
* Contributing to the establishment of various treatment protocols and prescription booklet services in regional hospitals.

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