News from the EMA

SECTION EDITOR

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First CAR-T cell medicine for mantle cell lymphoma

October 16, 2020 – The EMA has recommended granting a conditional marketing authorisation in the EU for Tecartus (autologous anti-CD19-transduced CD3+ cells) for the treatment of adult patients with a rare cancer of white blood cells called mantle cell lymphoma (MCL) when the symptoms or the disease come back (relapse) or when they are not responding (refractory) after two or more lines of systemic therapy.

Tecartus is the third CAR (Chimeric antigen receptor)-T cell medicine to be recommended for approval in the EU. CAR-Ts are advanced therapies for cancer, they belong to a new generation of personalised cancer immunotherapies that are based on collecting and modifying patients' own immune cells to treat their cancer.

MCL is an aggressive subtype of non-Hodgkin lymphoma that develops from abnormal B lymphocytes (B cells), a type of white blood cell. Its name derives from the fact that these cells originate from an area called the 'mantle zone' in lymph nodes.

The current standard of care for MCL includes treatment with stem cells taken from the patient's own body and a number of different therapy regimens. While patients with MCL can respond well to initial treatments, it is common that their disease returns or that they no longer respond to treatment.

There are some therapeutic options for patients with refractory/relapsed MCL, including a class of medicines known as Bruton's Tyrosine Kinase (BTK) inhibitors. However, treatment of patients with these forms of the disease is challenging due to the development of resistance to chemotherapy. Therefore, there is an unmet medical need for these patients.

To create each dose of Tecartus, the patient's blood is extracted and its T-cells, a type of white blood cell that help the body fight infection, are collected and genetically engineered to have a specific protein (CAR-T) that helps the body recognise and eliminate lymphoma cells. These modified immune cells are then infused back into the patient.

The safety and efficacy of Tecartus was studied in a multicentre clinical trial of adult patients with refractory or relapsed MCL. 74 patients received Tecartus with a 12-month follow-up that highlighted an objective response rate (ORR), i.e. the proportion of patients who experienced a certain tumour size reduction, of 84%, and a complete response, i.e. the disappearance of signs of cancer, of 59%.

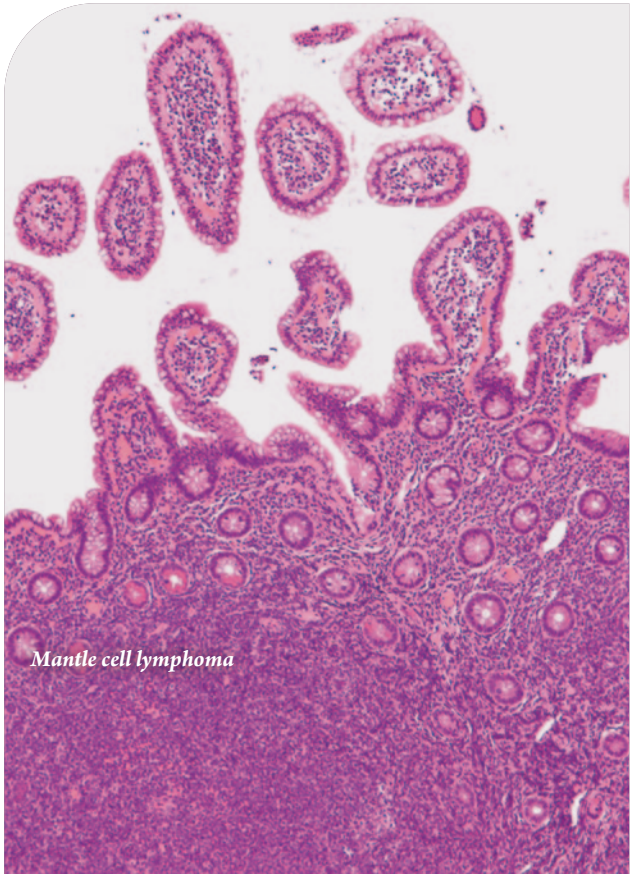
The most common side effects are cytokine release syndrome (CRS), which is a systemic response to the activation and proliferation of CAR-T-cells causing high fever and flu-like symptoms, infections, and encephalopathy, i.e. a brain disorder. The consequences of CRS can be life-threatening and, in some cases, even fatal. Monitoring and mitigation strategies for these side effects are described in the product information and in the risk management plan that is an integral part of the authorisation.

In its overall assessment of the available data, the Committee for Advanced Therapies (CAT), EMA's expert committee for cell- and gene-based medicines, found that the benefits of Tecartus outweighed the possible risks in the treatment of refractory/relapsed MCL in patients who had received more than two prior therapy regimens including BTK inhibitors.

The EMA's Committee for Medicinal Products for Human Use (CHMP) agreed with the CAT's assessment and positive opinion and recommended a conditional approval for this medicine. This is one of the EU's regulatory mechanisms to facilitate early access to medicines that fulfil an unmet medical need. This type of approval allows the Agency to recommend a medicine for marketing authorisation with less complete data than normally expected, in cases where the benefit of a medicine's immediate availability to patients outweighs the risk inherent in the fact that not all the data are yet available.

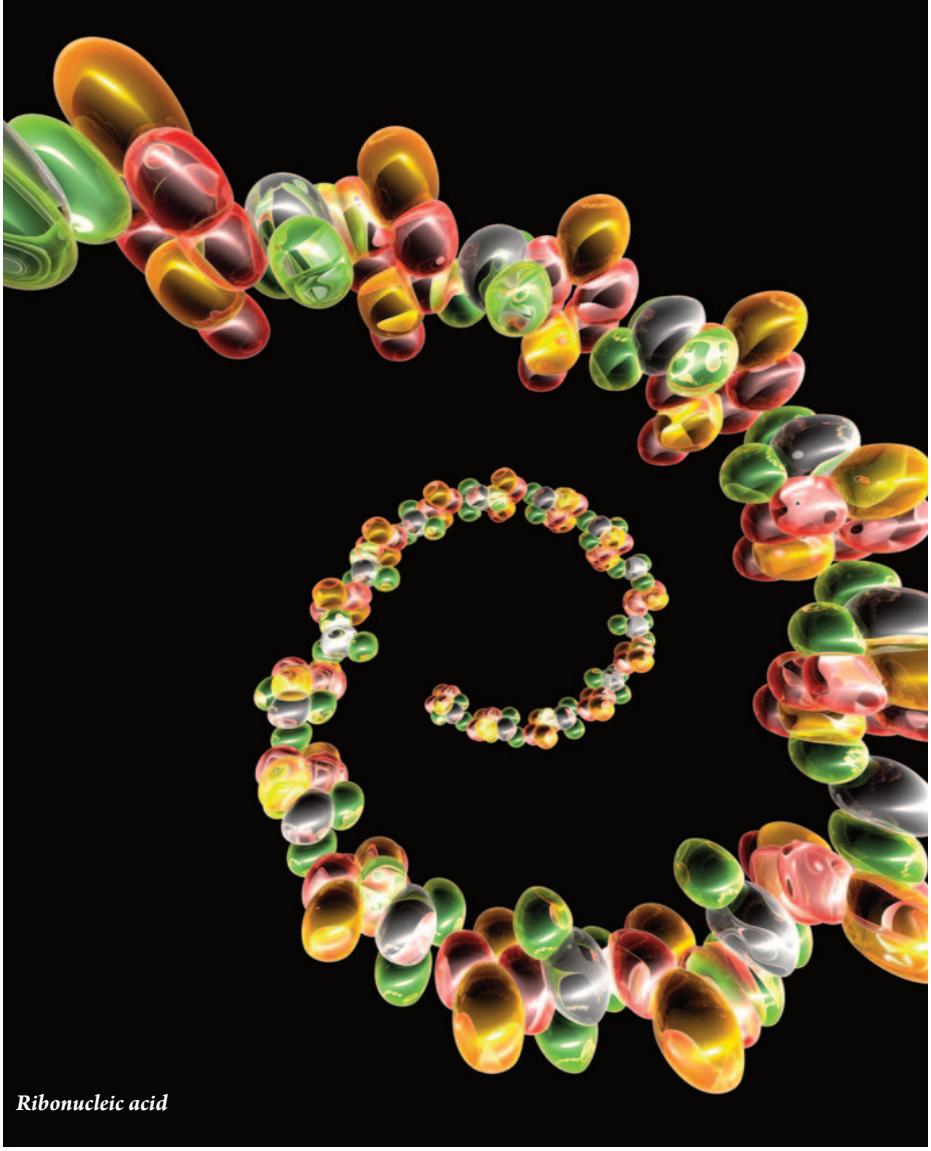
Additional efficacy and safety data are being collected through the submission of long-term follow-up data from the main study and through a registry-based study that will also collect data on the long-term efficacy and safety of the medicine in specific subgroups (elderly, females, patients with severe disease).

Tecartus was supported through EMA's PRIority MEdicines (PRIME) scheme, which provides early and enhanced scientific and regulatory support to medicines that have a particular potential to address patients' unmet medical needs. Tecartus was granted eligibility to PRIME in June 2018 for the treatment of adult patients with relapsed or refractory MCL.



Mantle cell lymphoma

First treatment for rare condition primary hyperoxaluria type 1: a small interfering ribonucleic acid



Ribonucleic acid

October 16, 2020 – EMA has recommended granting a marketing authorisation in the EU for Oxlumo (lumasiran) for the treatment of primary hyperoxaluria type 1 (PH1).

Primary hyperoxaluria is a rare inherited disorder characterised by the overproduction of oxalate. Oxalate can form calcium oxalate deposits, which can cause stones in the kidney and urinary tract (structures that carry urine) as well as injury to other organs such as the heart, eyes, bones, and skin. Characteristic symptoms of the disease include renal colic, blood in the urine, frequent urinary tract infections, and stomach pain.

PH1 is the most common and the most severe form of the disease, accounting for 80% of all cases. The condition is very rare with an estimated prevalence of 0.05 in 10,000 people in the EU.

There are currently no approved medicines for PH1 in the EU. Different treatments are used to prevent the accumulation of calcium oxalate such as dietary changes, drinking plenty of fluids, and taking vitamin B6. In certain cases, kidney and/or liver transplantation is required. Untreated PH1 leads to kidney failure, which is life-threatening.

Oxlumo will be available as a solution for injection (189 mg/ml). The active substance of Oxlumo is lumasiran, a small interfering ribonucleic acid that causes degradation of the messenger ribonucleic acid involved in the synthesis of the enzyme glycolate oxidase (GO) in the liver, leading to decreased GO enzyme levels in the body. This results in reduction of plasma and urinary oxalate levels, the underlying cause for the symptoms in patients with PH1.

The benefit of Oxlumo is its ability to reduce oxalate levels in the plasma and 24-hour urinary oxalate excretion, when compared to a placebo treatment. This was observed during a 6-month clinical trial involving 38 patients aged 6-60. In this study, treatment with Oxlumo resulted in normalisation of oxalate excretion in 52% of patients and near normalisation in 84% of patients. The most common side effects are injection site reactions and abdominal pain.

Oxlumo was accepted in EMA's PRIME scheme and has benefited from the extra support offered by the Agency to medicines that have a particular potential to address patients' unmet medical needs. EMA's human medicines committee (CHMP) reviewed the application for Oxlumo under its accelerated assessment procedure, which allows the speeding up of patients' access to medicines.

Cyberattack on EMA - update

December 22, 2020 – EMA has been the subject of a cyberattack, as reported on December 09, 2020. The ongoing investigation of this cyberattack was carried out by the Agency in close collaboration with law enforcement and other relevant entities and has revealed that the data breach was limited to one IT application. The perpetrators primarily targeted data related to COVID-19 medicines and vaccines and unlawfully accessed documents belonging to third parties. The companies concerned at this stage have been contacted and duly informed.

As the investigation proceeds, and all potentially suspicious activity is analysed, the Agency will ensure that any additional third party whose documents may have been subject to unauthorised access is notified. EMA will continue to provide information in due course, to the extent possible, given its duty towards the ongoing investigation.

The Agency and the European medicines regulatory network remain fully functional and timelines related to the evaluation and approval of COVID-19 medicines and vaccines are not affected.

Extra transparency measures for COVID-19 vaccines and therapeutics

October 30, 2020 – EMA has recommended implemented two further extra transparency measures for COVID-19 medicines, by publishing both the clinical data in support of the authorisation of Veklury (remdesivir) and information on the COVID-19 treatments and vaccines that have received scientific advice or informal guidance from EMA's pandemic Task Force (COVID-ETF). These are the latest measures in EMA's drive to maximise the transparency of its regulatory activities on treatments and vaccines for COVID-19.

The publication of clinical data for Veklury is in line with EMA's landmark policy to proactively publish clinical data supporting marketing authorisation applications. The Agency had to suspend the publication of clinical data at the end of 2018 as a result of its move from London to Amsterdam. It currently remains suspended due to ongoing business continuity linked to the COVID-19 pandemic and human resource constraints. EMA has decided to exceptionally publish clinical data for COVID-19 medicines given the unprecedented public interest for this information in the context of the ongoing pandemic.

The data package, consisting of 64 documents, is available on EMA's clinical data website and includes the clinical overview and summaries and the final reports from pharmacokinetic and phase I clinical studies, as well as interim study reports from phase III clinical studies and clinical data from the compassionate use programme. The data anonymisation report is also available. This explains the methods used to protect personal data, in line with a common approach agreed with Health Canada and the marketing authorisation holder for Veklury.

The list of medicines that have received scientific advice or guidance shows the stage of development when EMA gave its guidance. This guidance, which EMA provides at no cost, helps medicine developers prepare for an eventual marketing authorisation application, and can cover the best methods and study designs for generating robust data on a medicine's safety and effectiveness. It can also focus on quality aspects, such as manufacturing and testing, or on laboratory studies. The outcome of any consultation or advice from EMA is not binding on developers.

EMA and Health Canada publish clinical data used to support their authorisations of the Moderna COVID-19 vaccine share

March 2, 2021 — Openness and transparency are key to building confidence in COVID-19 vaccines. Today, EMA and Health Canada collaboratively published the full clinical data reviewed as part of their authorisations of the Moderna COVID-19 vaccine.

This international partnership highlights the shared commitment of both organisations to ensure the public has as much information as possible to make decisions regarding vaccination. Increasing access to clinical data can also have widespread benefits for the health care system and the research community. EMA and Health Canada are the only two jurisdictions in the world publishing this comprehensive information.

EMA and Health Canada are working together with manufacturers to expedite the publication of clinical information underpinning their authorisations for medicines and vaccines for COVID-19. The clinical data for the Pfizer-BioNTech COVID-19 vaccine is expected to be published shortly.

The clinical data package for the Moderna COVID-19 vaccine, presenting the interim safety and efficacy data generated in three clinical studies, is available on EMA's clinical data website and Health Canada's Public Release of Clinical Information portal.

The data anonymisation report is also part of the data package. It provides an explanation of the methods used to protect personal data in the clinical reports.

EMA publishes safety monitoring plan and guidance on risk management planning for COVID-19 vaccines

November 13, 2020 – EMA and the national competent authorities (NCAs) in EU Member States have prepared a safety monitoring plan for COVID-19 vaccines. The plan outlines how relevant new information emerging after the authorisation and uptake of COVID-19 vaccines in the pandemic situation will be collected and promptly reviewed.

The safety of COVID-19 vaccines will be monitored according to the guidance set out by EMA and NCAs in the good pharmacovigilance practices (GVP), that applies to all medicines. In view of the extraordinary circumstances, though, EU authorities have planned several activities that will apply specifically to COVID-19 vaccines.

Through the implementation of these activities, the EU medicines regulatory network will assess any safety data emerging from a range of different sources (spontaneous reporting, observational studies, etc.). Any potential safety concerns identified will be addressed by taking appropriate regulatory action to safeguard individual and public health and communicating with the public in a transparent and timely manner.

The plan comprises new reporting obligations for companies that will have to submit monthly safety reporting summaries in addition to the regular updates foreseen by the legislation. Furthermore, the plan details the scientific studies already in place to monitor the safety, effectiveness, and coverage of COVID-19 vaccines after their authorisation. Lastly, it details the exceptional transparency measures set up by EMA as well as how the Agency plans to engage with a wide range of stakeholders.

In this context, EMA has also published guidance to support pharmaceutical companies' preparation of risk management plans (RMPs) for COVID-19 vaccines. As for any medicine, companies applying for a marketing authorisation for COVID-19 vaccines must submit RMPs. The RMP explains how the company must monitor and report on the safety of the vaccine once authorised, and what measures it must put in place to further characterise and manage risks. RMPs are updated as new information becomes available. The RMP guidance for COVID-19 vaccines complements the existing guidelines on the RMP format in the EU and guidance on good pharmacovigilance practices, which apply to all medicines. Additional specific considerations in this guidance address, for example:

- Further information on vaccine safety that might be generated after the marketing authorisation in special populations, such as the elderly, children, or patients with co-morbidities;
- Core requirements for lists of adverse events of special interest, methods used for signal detection, and follow-up of any safety signals identified in clinical trials;
- Submission of monthly summary safety reports by marketing authorisation holders to EMA in addition to the usual periodic safety update reports;
- traceability tools that can help record who has received which vaccine and from which batch.

All activities that companies include in the RMP for a COVID-19 vaccine should take into account EMA's infrastructure to support the monitoring of the efficacy and safety of COVID-19 treatments and vaccines when used in day-to-day clinical practice.

Science Communication on Social Media: Good Practices

QUEST stands for **QU**ality and **E**ffectiveness in **S**cience and **T**echnology communication (https://questproject.eu/). The group consists of a team of experts, scholars, and media professionals across Europe who have come together to investigate current issues in science communication. Their objective is to develop tools, recommendations, and guidelines for communicators and practitioners working in the fields of journalism, social media, and museums.

One of their deliverables is the recommendation document Science Communication on Social Media: Good Practices, available at: https://questproject.eu/social-media-improving-science-communication-by-the-tools-of-science/

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