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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Vaccinia GM-CSF/TK-deactivated virus for the treatment of hepatocellular carcinoma

On 26 November 2009, orphan designation (EU/3/09/700) was granted by the European Commission to Sirius Regulatory Consulting Limited, United Kingdom, for vaccinia GM-CSF/TK-deactivated virus for the treatment of hepatocellular carcinoma.

The sponsorship was transferred to Transgene S.A., France, in September 2011.

What is hepatocellular carcinoma?

Hepatocellular carcinoma is a primary cancer of the liver (a cancer that starts in the liver, rather than a cancer that has spread to the liver from another location in the body). It is more common in men than in women, and occurs mostly in people who have scarring of the liver (cirrhosis) or after infection with the hepatitis B or C viruses. Symptoms of the disease include pain and swelling in the tummy, weight loss, weakness, loss of appetite and nausea (feeling sick).

Hepatocellular carcinoma is a severe and life-threatening disease that is associated with very poor long-term survival.

What is the estimated number of patients affected by the condition?

At the time of designation, hepatocellular carcinoma affected approximately 1 in 10,000 people in the European Union (EU)*. This is equivalent to a total of around 50,000 people, and is below the threshold for orphan designation, which is 5 people in 10,000. This is based on the information provided by the sponsor and knowledge of the Committee for Orphan Medicinal Products (COMP).

What treatments are available?

At the time of designation, several medicines were authorised in the EU for the treatment of hepatocellular carcinoma. The choice of treatment depended mainly on how advanced the disease was. Surgery to remove the tumour and liver transplantation were the only ways to cure the cancer, but

* Disclaimer: For the purpose of the designation, the number of patients affected by the condition is estimated and assessed on the basis of data from the European Union (EU 27), Norway, Iceland and Liechtenstein. This represents a population of 504,800,000 (Eurostat 2009).

could only be used in very few patients. Other treatments included radiotherapy (treatment with radiation), chemotherapy (medicines to treat cancer) and immunotherapy (treatment by stimulation of the immune system, the body's natural defences).

The sponsor has provided sufficient information to show that vaccinia GM-CSF/TK-deactivated virus might be of significant benefit for patients with hepatocellular carcinoma because it works in a different way to existing treatments and because early studies indicate that it could be used in combination with existing treatment options to improve the overall outcome of patients with this condition. These assumptions will need to be confirmed at the time of marketing authorisation, in order to maintain the orphan status.

How is this medicine expected to work?

Vaccinia GM-CSF/TK-deactivated virus is an 'oncolytic' virus, a type of virus that has been modified to target cancer cells. The virus has been modified so that it contains an additional gene called GM-CSF that enhances the anticancer effects of the virus. It has also had one of its own genes called tyrosine kinase (TK) inactivated. This means that the virus cannot produce its own TK protein, so it can only reproduce itself within cancer cells, which usually contain high levels of TK.

When the medicine is injected into a patient with hepatocellular carcinoma, the virus is expected to reproduce in the cancer cells and produce the GM-CSF protein, which stimulates the immune system to attack the cancerous cells. The virus is then expected not only to spread locally to the neighbouring cancer cells, but also to be released into the bloodstream and reach distant cancer cells.

What is the stage of development of this medicine?

The effects of vaccinia GM-CSF/TK-deactivated virus have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with the designated product in patients with hepatocellular carcinoma were ongoing.

At the time of submission, vaccinia GM-CSF/TK-deactivated virus was not authorised anywhere in the EU for hepatocellular carcinoma or designated as orphan medicinal product elsewhere for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 7 October 2009 recommending the granting of this designation.

Opinions on orphan medicinal product designations are based on the following three criteria:

- the seriousness of the condition;
- the existence of alternative methods of diagnosis, prevention or treatment;
- either the rarity of the condition (affecting not more than 5 in 10,000 people in the EU) or insufficient returns on investment.

Designated orphan medicinal products are products that are still under investigation and are considered for orphan designation on the basis of potential activity. An orphan designation is not a marketing authorisation. As a consequence, demonstration of quality, safety and efficacy is necessary before a product can be granted a marketing authorisation.

For more information

Sponsor's contact details:

Transgene S.A.
Boulevard Gonthier d'Andernach
Parc d'Innovation CS80166
67405 Illkirch Graffenstaden Cedex
France
Telephone: +33 3 88 27 91 90
Telefax: +33 3 88 27 91 41
E-mail: communication@transgene.fr

For contact details of patients' organisations whose activities are targeted at rare diseases see:

- [Orphanet](#), a database containing information on rare diseases which includes a directory of patients' organisations registered in Europe.
- [European Organisation for Rare Diseases \(EURORDIS\)](#), a non-governmental alliance of patient organisations and individuals active in the field of rare diseases.

Translations of the active ingredient and indication in all official EU languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Vaccinia GM-CSF/TK-deactivated virus	Treatment of hepatocellular carcinoma
Bulgarian	Vaccinia GM-CSF/TK деактивиран вирус	Лечение на хепатоцелуларен карцином
Czech	Vakcína GM-CSF/TK deaktivovaný virus	Léčba hepatocelulárního karcinomu
Danish	Vaccinia GM-CSF/TK deaktiveret virus	Behandling af hepatocellulært carcinom
Dutch	Vaccinia GM-CSF/TK gedeactiveerd virus	Behandeling van hepatocellulair carcinoom
Estonian	Vaktsiiniaviirus GM-CSF/TK deaktiveeritud viiruse	Hepatotsellulaarse kartsinoomi ravi
Finnish	Vaccinia GM-CSF/TK-deaktivoitu Vaccinia-virus	Hepatosellulaarisen karsinooman hoito
French	Vaccine GM-CSF/ virus TK-désactivé	Traitement du carcinome hépatocellulaire
German	Vaccinia GM-CSF/TK-deaktiviertes virus	Behandlung des Leberzellkarzinoms
Greek	Απενεργοποιημένος GM-CSF/TK ιός δαμαλίδος λύμφης	Θεραπεία του ηπατοκυτταρικού καρκινώματος
Hungarian	Vaccinia GM-CSF/TK inaktívált vírus	Hepatocelluláris carcinoma kezelése
Italian	Virus vaccिनico transgenico per GM-CSF e TK-disattivato	Trattamento del carcinoma epatocellulare
Latvian	Deaktivēta GM-CSF/TK vīrusa vakcīna	Hepatocellulāras karcinomas ārstēšana
Lithuanian	Vaccinia GM-CSF/TK deaktyvuotas virusas	Hepatoceliulinės karcinomos gydymas
Maltese	Virus tal-vaccinia deattivat bil-GM-CSF/TK	Kura tal-karcinoma epatoċellulari
Polish	Wirus krowianki ze wstawionym genem dla GM-CSF i wyłączonym genem dla TK	Leczenie raka wątrobowokomórkowego
Portuguese	Vírus da Vacína GM-CSF/TK inactivado	Tratamento do carcinoma hepatocelular
Romanian	Virus vaccinal GM-CSF/TK dezactivat	Tratamentul carcinomului hepatocelular
Slovak	GM-CSF/TK deaktivovaný vakcína vírus	Liečba hepatocelulárneho karcinómu
Slovenian	Vakcinija GM-CSF/TK deaktiviran virus	Zdravljenje hepatocelularnega karcinoma
Spanish	Virus de la vacuna con timidina kinasa (TK) desactivada, que expresa GM-CSF	Tratamiento del carcinoma hepatocelular
Swedish	Vaccinia GM-CSF/TK deaktiverats virus	Behandling av hepatocellulärt carcinom
Norwegian	Vaccinia GM-CSF/TK deaktivert virus	Behandling av hepatocellulært karsinom
Icelandic	Kúabólu GM-CSF/TK afvirkjuð veira	Meðferð við lifrarfrumukrabbameini

¹ At the time of designation