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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Autologous CD4+ and CD8+ T cells transduced with lentiviral vector containing an affinity-enhanced T-cell receptor targeting the New York esophageal antigen-1 for the treatment of soft tissue sarcoma

On 14 July 2016, orphan designation (EU/3/16/1694) was granted by the European Commission to Adaptimmune Limited, United Kingdom, for autologous CD4+ and CD8+ T cells transduced with lentiviral vector containing an affinity-enhanced T-cell receptor targeting the New York esophageal antigen-1 for the treatment of soft tissue sarcoma.

What is soft tissue sarcoma?

Soft tissue sarcoma is a cancer that affects the soft, supportive tissues of the body. It can occur in muscles, blood vessels, fat tissue or in other tissues that support, surround and protect organs. Patients with soft tissue sarcoma do not usually have symptoms in the early stages of the disease. First symptoms appear when the tumour grows large enough to cause swelling and pain.

Soft tissue sarcoma is a long-term debilitating and life-threatening disease, particularly when the cancer has spread to other parts of the body.

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

At the time of designation, soft tissue sarcoma affected approximately 2.8 in 10,000 people in the European Union (EU). This was equivalent to a total of around 144,000 people[*], and is below the ceiling for orphan designation, which is 5 people in 10,000. This is based on the information provided by the sponsor and the knowledge of the Committee for Orphan Medicinal Products (COMP).

What treatments are available?

At the time of designation, the main treatment for early-stage soft tissue sarcoma was surgery. For large sarcomas, surgery was usually followed by radiotherapy (treatment with radiation) and

[*]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 28), Norway, Iceland and Liechtenstein. This represents a population of 513,700,000 (Eurostat 2016).

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chemotherapy (medicines to treat cancer) to kill any cancer cells that were left behind. Several medicines were authorised in the EU for the treatment of soft tissue sarcoma including doxorubicin.

The sponsor has provided sufficient information to show that medicine might be of significant benefit for patients with soft tissue sarcoma. The response rate in early studies with the medicine compared well with response rates seen in medical literature with other authorised treatments. This assumption 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?

This medicine is made up of T cells taken from the patient. T cells are cells of the immune system (the body's natural defences) that kill infected or abnormal cells. To make this medicine, the T cells are modified by a virus known as a 'lentivirus'. The virus carries a gene that enables the T cells to produce a receptor that recognises the protein NY-ESO-1 as foreign. NY-ESO-1 is found at high levels on cells in many soft tissue sarcomas. When these modified T cells are given back to the patient, they are expected to recognise and kill cancer cells producing NY-ESO-1, thus reducing the growth and spread of the tumour.

The virus has been designed so that it does not enter other types of cells and cannot reproduce itself and cause disease in the body.

What is the stage of development of this medicine?

The effects of the medicine have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with the medicine in patients with various cancers were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for soft tissue sarcoma. Orphan designation has been granted in the United States for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 16 June 2016 recommending the granting of this designation.

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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:

Contact details of the current sponsor for this orphan designation can be found on EMA website, on the medicine's rare disease designations page.

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 languages[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	Autologous CD4+ and CD8+ T-cells transduced with lentiviral vector containing an affinity-enhanced T-cell receptor targeting the New York esophageal antigen-1	Treatment of soft tissue sarcoma
Bulgarian	Автоложни CD4+ и CD8+ Т клетки трансдуцирани с лентивирусен вектор, съдържащи Т-клетъчен рецептор с повишен афинитет насочен към Ню Йорк хранопровода антиген-1	Лечение на сарком на меките тъкани
Croatian	Autologne CD4+ i CD8+ T stanice transducirane lentivirusnim vektorom koji sadrži T stanični receptor s poboljšanim afinitetom koji cilja New York ezogagusni antigen-1	Liječenje sarkoma mekih tkiva
Czech	Autologní CD4+ a CD8+ T buňky transdukované lentivirálním vektorem se zvýšenou affinitou T–buněčného receptoru cílícího New York jícnový antigen-1	Léčba sarkomu měkkých tkání
Danish	Autolog CD4+ og CD8+ T celler transduceret med lentiviralvektor indeholdende en affinitetsforbedret T-celle receptor målrettet mod New York øsofageal antigen-1	Behandling af bløddelssarkom
Dutch	Autologe CD4+ en CD8+ T-cellen getransduceerd met lentivirale vector welke een affiniteit-“enhanced” T-cel receptor gericht op het New York oesofagaal antigen-1 bevat	Behandeling weke delen sarcoom
Estonian	Autoloogsede CD4+ja CD8+T rakud, mida on transdutseeritud lintiviirus vektoriga, mis sisaldab suurenenud afiinsusega T-raku retseptorit, mis on suunatud New Yorgi söögitoru antigeenile 1,	Pehmete kudede sarkoomi ravi
Finnish	Autologiset CD4+ ja CD8+ T-solut, joihin on lentivirusvektorin avulla istutettu affiniteetiltaan parannettu T-solureseptori, jonka kohteena on New York ruokatorven 1 antigeeni	Pehmytkudossarkooman hoito
French	Cellules T CD4+ et CD8+ transduites avec un vecteur lentiviral contenant un récepteur d'affinité accrue des cellules T pour cibler l'antigène-1 New York oesophagique	Traitement des sarcomes des tissus mous
German	Autologe CD4+ und CD8+ T-Zellen tranduziert mit einem viralen Vektor der einen T-Zell-Rezeptor mit erhöhter Affinität gegen das New York Esophageal Antigen-1	Behandlung des Weichteilsarkoms
Greek	Αυτόλογα Τ κύτταρα CD4+ και CD8+ διαμολυσμένα με φορέα λεντοϊού που φέρει Τ κυτταρικό υποδοχέα ενισχυμένης συγγένειας προς το οισοφαγικό αντιγόνο-1 της Νεας Υόρκης	Θεραπεία του σαρκώματος των μαλακών ιστών
Hungarian	New York esofagális antigén-1-et célzó, fokozott affinitású T-sejt receptort tartalmazó, lentivirális vektorral transzdukált autológ CD4+ és CD8+ T-sejtek	Lágy szöveti sarcoma kezelése

[1] At the time of designation

Language	Active ingredient	Indication
Italian	CD4+ e CD8+ T autologhi trasdotti con un vettore lentivirale contenente un recettore delle cellule T ad'affinità-potenziata diretto verso l'antigene tumorale–New York-1 esofageo	Trattamento dei sarcomi dei tessuti molli
Latvian	Autologas CD4+ un CD8+ T šūnas, kas transducētas ar lentivīrusa vektoru, kas satur paaugstinātas afinitātes pret New York barības vada antigēnu-1 vērstu T šūnu receptoru	Mīksto audu sarkomas ārstēšana
Lithuanian	Autologinės CD4+ ir CD8+ T ląstelės, transdukuotos su lentivirusiniu vektoriumi, turinčiu padidinto jautrumo T ląstelių receptorių, nukreiptą prieš Niujorko stemplės antigeną-1	Minkštųjų audinių sarkomos gydymas
Maltese	Ċelloli T awtologi CD4+ u CD8+ trasformati permezz ta' vettur lentivirali li fih riċettur għaċ-ċelluli T b'affinita mkabbra immirat għall-antigen 1 tal-esofagu New York	Kura tas-sarkoma tat-tessuti rotob
Polish	Autologiczne komórki T CD4+ i CD8+ pozytywne transdukowane wektorem lentiwirusowym zewierającym receptor komórek T o zwiększonym powinowactwie, skierowany przeciw antygenowi przełyku New York 1	Leczenie mięsaków tkanek miękkich
Portuguese	Células T CD4+ e CD8+ autólogas transduzidas com um vetor lentiviral contendo um receptor de células T com afinidade aumentada para o New York esophageal antigen-1	Tratamento do sarcoma dos tecidos moles
Romanian	Celule T autologe CD4+ şi CD8+ transduse cu un vector lentiviral ce conţine un receptor pentru celule T cu afinitate crescută ce ţinteşte antigenul esofagian New York 1	Tratamentul sarcomului ţesuturilor moi
Slovak	Autológne CD4+ a CD8+ T bunky transdukované s T bunkovým receptorom s vylepšenou afinitou zameriavajúci sa na New York ezofageálny antigén-1	Liečba sarkómu mäkkých tkanív
Slovenian	Autologne CD4+ and CD8+ T-celice, transducirane z lentivirusnim vektorjem, ki imajo zvečano afiniteto za T-celični receptor za New York ezofagealni antigen-1	Zdravljenje sarkoma mehkih tkiv
Spanish	Células CD4+ y CD8+ T autólogas diseñado con un receptor de mayor afinidad de la célula T que cibla el antígeno-1-Nueva York del esofago	Tratamiento del sarcoma de tejidos blandos
Swedish	CD4+ och CD8+ T-celler konstruerade med en affinitet-förbättrade T-cell receptor riktad mot cancer-testis tumör antigenet New York esofagalt antigen-1	Behandling av mjukdelssarkom
Norwegian	Autologe CD4+ og CD8+ Tceller transdusert med lentoviral vektor inneholdende en affinitets-forbedret T-celle reseptor mot New York esofagealt antigen-1	Behandling av bløtvevssarkom
Icelandic	Samgena CD4 og CD8 T-frumur sem eru flutter með lentiveiru ferju sem inniheldur sæknibættan T-frumu viðtaka sem beinist gegn New York vélinda antigeni-1	Meðferð við mjúkvefjasarkmeini