Novartis receives approval for Kymriah® (tisagenlecleucel) by Health Sciences Authority as Singapore's first commercially approved CAR-T therapy

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- Kymriah, the first chimeric antigen receptor T-cell (CAR-T) therapy approved in Singapore, is indicated as a one-time treatment manufactured individually for each patient.
- Novartis works closely with qualified centres to deliver this treatment for eligible relapsed/refractory (r/r) pediatric and young adult B-cell ALL and adult r/r DLBCL patients.
- The approval represents the first commercial CAR-T therapy in Southeast Asia, putting Singapore at the forefront in changing the landscape of cancer care in the region.
- The treatment is now available in Singapore General Hospital for adult r/r DLBCL patients and young adult r/r B-cell ALL patients while discussions are on-going for the National University Hospital to treat adult r/r DLBCL patients as well as r/r pediatric and young adult B-cell ALL patients.

Singapore, 9 March, 2021 – Novartis announced today that the Health Sciences Authority (HSA) has approved Kymriah (tisagenlecleucel) as the first commercial chimeric antigen receptor T-cell (CAR-T) therapy in Singapore under the new cell, tissue and gene therapy products (CTGTP) regulatory framework. Kymriah, a CD19-directed genetically modified autologous T-cell immunocellular therapy, is approved to treat two life-threatening cancers that have limited treatment options and historically poor outcomes, addressing the critical need for new therapies for these patients.

HSA approved Kymriah for the treatment of pediatric and young adult patients from 2 to 25 years of age with B-cell acute lymphoblastic leukemia (ALL) that is refractory, in relapse post-transplant or in second or later relapse; and for the treatment of adult patients with relapsed or refractory (r/r) diffuse large B-cell lymphoma (DLBCL) after two or more lines of systemic therapy[1].

The approval was based on the review of two global registration CAR-T clinical trials, JULIET and ELIANA. In these trials, Kymriah demonstrated strong and durable response rates and a consistent safety profile in two difficult-to-treat patient populations[1,2,3].

Kymriah is an individualised treatment that modifies a patient's own T-cells to fight and kill cancer cells. Bringing this new innovative therapy to Singapore requires collaboration among many health system stakeholders. This includes obtaining regulatory approval, the validation and training of qualified treatment centres for the appropriate indications, and integrating a delivery system that did not previously exist for individualised treatments to ensure safe and seamless delivery of Kymriah to patients.

Singapore General Hospital (SGH) is the first Kymriah treatment centre to become operational in Southeast Asia to treat adult r/r DLBCL and young adult r/r B-cell ALL patients. Novartis is currently in discussions with the National University Hospital (NUH) to expand the availability of Kymriah for both adult r/r DLBCL and pediatric and young adult r/r B-cell ALL patients. The approval of Kymriah in Singapore and the presence of these regional centers of excellence will enable the city state to help an underserved patient population in the

Southeast Asia region where treatment unmet needs are present.

Professor William Hwang, Medical Director of the National Cancer Centre Singapore, Head of SingHealth Duke-NUS Cell Therapy Centre, Senior Consultant of SingHealth Duke-NUS Blood Cancer Centre, and Senior Consultant for Haematology at SGH said, “CAR-T therapy is a major advancement in the emergence of immune-based strategies and is a significant step forward in individualised cancer treatment. This therapy shows great promise as a life-saving treatment and offers new hope to patients with blood cancers and disorders.”

“80-85% of acute lymphoblastic leukemia patients are cured with frontline chemotherapy. However, for 15% of patients, when front-line therapies have failed, the new therapies are needed. This regulatory approval for the wider availability of treatment options including CAR-T therapy is welcome.” said **Professor Allen Yeoh, Head and Senior Consultant of the Division of Paediatric Haematology and Oncology of the Khoo Teck Puat-National University Children's Medical Institute, NUH and National University Cancer Institute, Singapore (NCIS)**.

Meeting unmet patient needs

ALL is a type of cancer that affects the blood and bone marrow[5]. ALL is the most common type of childhood leukemia[4], and for at clinically high risk patients who relapse from standard of care therapies, the outlook is poor[6]. These poor outcomes occur in more than half of the cases of relapsed ALL patients, in spite of patients having to undergo multiple treatments, including chemotherapy, radiation, targeted therapy, or stem cell transplant, and further highlights the need for new treatment options[6].

DLBCL is an aggressive, complex and difficult to treat form of non-Hodgkin lymphoma, accounting for up to 40% of all cases globally[7]. For patients who relapse or do not respond to existing treatment options, there are limited treatment options that provide durable responses, and survival rates are low for the majority of patients due to ineligibility for autologous stem cell transplant (ASCT) or unresponsiveness to salvage chemotherapy[8].

Pioneering Technology

CAR-T therapy represents a significant step forward in treating these cancers and is the embodiment of personalized medicine. Kymriah is manufactured individually for each patient using their own cells. It is not a pill or chemotherapy, but instead it is an individualized treatment produced via pioneering technology and a sophisticated manufacturing and supply chain process.

The therapy first requires drawing blood from the patient via apheresis and separating out the T-cells. The T-cells are then cryopreserved and transported to the Novartis manufacturing facility. Next, using a disarmed virus, the patient’s T-cells are genetically engineered to produce receptors on their surface called chimeric antigen receptors (CARs). These special receptors allow the T-cells to recognize and attach to a specific protein or antigen found on cancerous B-cells and other B-cells expressing a specific antigen. The CAR T-cells then undergo expansion in the laboratory. The resulting therapy is transported from the Novartis manufacturing facility back to the treatment centre and administered to the patient via infusion in one single session. The infused CAR T-cells recognize and kill cancer cells that harbor the antigen on their surfaces, and act as a living drug by further multiplying in the patient's body to destroy the future appearance of cancerous B-cells.

“At Novartis, we have a long history of being at the forefront of transformative cancer treatment, and we are continuously looking for innovative ways to treat blood cancers.” said **Kevin Zou, Head of Oncology, Asia Pacific and Country President of Novartis Singapore**. “Kymriah, a one-time, individualised cancer treatment, is a concrete demonstration of our commitment to develop innovative practice-changing technologies. This approval is a defining moment for many patients in Singapore and the region who are in need of new treatment

options.”

About CAR-T therapy

CAR-T (Chimeric Antigen Receptor – T cell) therapy is different from typical small molecule or biologic therapies because it is manufactured for each individual patient using their own cells. During the treatment process, T cells are drawn from a patient's blood and reprogrammed in the laboratory to create T cells that are genetically coded to recognise and fight the patient's cancer cells.

About the ELIANA Trial[3]

ELIANA is the first pediatric global CAR-T therapy registration trial, examining patients in 25 centers in 11 countries across the US, Canada, Australia, Japan and the EU, including: Austria, Belgium, France, Germany, Italy, Norway and Spain. In 2012, Novartis and the University of Pennsylvania entered into a global collaboration to further research, develop and commercialize CAR-T therapies, including Kymriah, for the investigational treatment of cancers.

About the JULIET Trial[2]

JULIET is the first multi-center global registration study for tisagelecleucel in adult patients with r/r DLBCL. JULIET, led by researchers at the University of Pennsylvania, is the largest and only registration study examining a CAR-T cell therapy in DLBCL, enrolling patients from 27 sites in 10 countries.

Novartis Leadership in Immuno-Oncology

Novartis is at the forefront of investigational immunocellular therapy as the first pharmaceutical company to initiate global CAR-T trials, and has significantly invested in CAR-T research and worked with pioneers in the field. Tisagenlecleucel is the cornerstone of this strategy. Active research programmes are underway targeting other hematologic malignancies and solid tumours, and include efforts focused on next generation CAR-Ts with evolved manufacturing schemes and gene edited cells. For more information, please visit https://www.novartis.com/our-focus/cell-and-gene-therapy/car-t

Novartis CAR-T Manufacturing

The Novartis global CAR-T manufacturing footprint spans seven facilities, across four continents. This comprehensive, integrated footprint strengthens the flexibility, resilience and sustainability of Novartis manufacturing and supply chain. Commercial and clinical trial manufacturing is now ongoing at Novartis-owned facilities in Stein, Switzerland, Les Ulis, France and Morris Plains, New Jersey, USA, as well as at the contract manufacturing sites at Fraunhofer Institute for Cell Therapy and Immunology (Fraunhofer-Institut für Zelltherapie und Immunologie) facility in Leipzig, Germany, Foundation for Biomedical Research and Innovation (FBRI) in Kobe, Japan, and now Cell Therapies in Melbourne, Australia. Manufacturing production at Cellular Biomedicine Group in China is forthcoming.

Please see full Prescribing Information here for Kymriah® for more information.

About Novartis

Novartis is reimagining medicine to improve and extend people’s lives. As a leading global medicines company, we use innovative science and digital technologies to create transformative treatments in areas of great medical need. In our quest to find new medicines, we consistently rank among the world’s top companies investing in research and development. Novartis products reach nearly 800 million people globally and we are finding innovative ways to expand access to our latest treatments. About 110,000 people of more than 140 nationalities work at Novartis around the world. Find out more at https://www.novartis.com

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List of links present in page

- https://www.novartis.com/sg-en/sg-en/news/media-releases/novartis-receives-approval-kymriah-tisagenlecleucel-health-sciences-authority-singapores-first-commercially-approved-car-t-therapy
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