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Kymriah® (tisagenlecleucel), CAR-T therapy from Novartis, receives TGA approval for treating two aggressive blood cancers.

- *Kymriah® is an immunocellular therapy that is a one-time treatment manufactured individually for each patient using the patient's own T cells, genetically reengineered and programmed to recognise and destroy cancer cells.*

- *Kymriah® is approved for the treatment of relapsed or refractory patients with paediatric B-cell acute lymphoblastic leukaemia (ALL) and adult diffuse large B-cell lymphoma (DLBCL)[1].*

- *Kymriah® could be a treatment option for about 50 paediatric and young adult ALL patients and 420 adult DLBCL patients who relapse or do not respond to initial therapy[2].*

- *Kymriah® is the only chimeric antigen receptor T cell (CAR-T) therapy to receive TGA approval in Australia[1].*

Sydney, December 19, 2018 – Novartis today announced that the Therapeutic Goods Administration (TGA) has approved Kymriah® (tisagenlecleucel, formerly CTL019). The approved indications are for the treatment of paediatric and young adult patients up to 25 years of age with B-cell precursor acute lymphoblastic leukaemia (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 diffuse large B cell lymphoma (DLBCL) after two or more lines of systemic therapy[1]. Kymriah is not indicated for patients with primary central nervous system lymphoma[1].

Kymriah 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 and other B cells expressing a particular antigen.

"The TGA approval of Kymriah is a defining moment for patients in Australia with these aggressive blood cancers," said Lauren Carey, General Manager Oncology and Country President, Novartis Australia and New Zealand. "Kymriah is a one-time treatment that helps address significant treatment gaps and a profound unmet need for patients."

"This CD19 CAR-T may change the treatment paradigm for relapsed diffuse large B-cell lymphoma and relapsed acute lymphoblastic leukaemia," said Dr Michael Dickinson, Haematologist, Peter MacCallum Cancer Centre. "The TGA's considerations were based on the review of the two global registration CAR-T clinical trials, JULIET and ELIANA, which included patients from Australia. In these trials, Kymriah delivered complete and durable response rates for

some patients who otherwise had little chance of remission. The TGA's approval is a major milestone for Kymriah in Australia, and each step made towards future availability of this treatment for patients, is welcome."

Acute lymphoblastic leukaemia (ALL) is a type of cancer that affects the blood and bone marrow. In Australia, ALL is the most common type of childhood leukaemia[3], and for patients who relapse from standard of care therapies, the outlook is poor[4]. These poor outcomes occur 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[4].

Diffuse large B-cell lymphoma (DLBCL) is an aggressive, complex and difficult to treat form of non-Hodgkin lymphoma, accounting for up to 40% of all cases globally[5]. For patients who relapse or don't respond to initial therapy, there are limited treatment options that provide durable responses, and survival rates are low for patients who are ineligible for autologous stem cell transplant (ASCT) or because salvage chemotherapy or ASCT have failed[6].

"Australia is one of the first places in the world to issue a regulatory approval of Kymriah, after the United States and Europe," said Richard Vines, Founder and Chairman, Rare Cancers Australia. "We have seen a number of Australians travelling to United States for this treatment and today's announcement gives hope to patients and their families who are running out of treatment options."

"We are entering a transformative time in cancer care. Novartis is delighted about today's announcement and the meaningful difference this therapy will make to patients in Australia," Ms Carey added. "The next step is to ensure public funding for Kymriah so it is accessible for all eligible patients and we are committed to working with the Australian Government to achieve this as soon as possible."

Kymriah® (tisagenlecleucel) Important Safety information[1]

Warning: Cytokine Release Syndrome (CRS), including fatal or life threatening reactions, occurred in patients receiving KYMRIAH. Do not administer KYMRIAH to patients with active infection or inflammatory disorders. Treat severe or life threatening CRS with tocilizumab as per the CRS management algorithm.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE: Cytokine release syndrome; Neurological events; Infections and febrile neutropenia; Prolonged cytopenias; Secondary malignancies; Hypogammaglobulinemia; Live vaccines; Tumour lysis syndrome; Blood, organ, tissue and cell donation; Active central nervous system (CNS) leukaemia or lymphoma; Concomitant disease such as patients with a history of active CNS disorder or inadequate renal, pulmonary or cardiac function; Prior bone marrow transplant; HIV, Hepatitis B, Hepatitis C and viral reactivation; Prior treatment with an anti-CD19 therapy; Effects on laboratory tests; Use in the elderly and paediatric use; Reasons to delay treatment such as Unresolved serious adverse reactions, Active uncontrolled infection; active chronic GVHD, Significant clinical worsening of leukaemia burden or rapid progression of lymphoma with unstable clinical presentation following lymphodepleting chemotherapy; Patient information regarding adverse event symptoms.

References

[1] Product Information will be available on the TGA website pending finalisation. Kymriah® is now included on the ARTG.
[2] Data on File
[3] Leukaemia Foundation. Acute Lymphoblastic Leukaemia. Available at: https://www.leukaemia.org.au/disease-information/leukaemias/acute-lymphoblastic-leukaemia/. Accessed December 2018
[4] Ronson, A., Tvito, A., Rowe, JM., "Treatment of Relapsed/Refractory Acute Lymphoblastic Leukemia in Adults." Current Oncology Reports, 2016 Jun;18(6):39.
[5] World Health Organization. Diffuse large B-cell lymphoma. Review of cancer medicines on the WHO list of essential medicines. Available at: http://www.who.int/selection_medicines/committees/expert/20/applications/DiffuseLargeBCellLymphoma.pdf. Accessed December 2018
[6] Crump M, Neelapu S, Farooq U, Van Den Neste E, Kuruvilla J et al. (2017) Outcomes in refractory diffuse large B-cell lymphoma: results from the international SCHOLAR-1 study. Blood. E-pub ahead of print August 03.

About Novartis

Novartis provides innovative healthcare solutions that address the evolving needs of patients and societies. Headquartered in Basel, Switzerland, Novartis offers a diversified portfolio to best meet these needs: innovative medicines, cost-saving generic and biosimilar pharmaceuticals and eye care.

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