

Novartis announces CTL019 data published in NEJM demonstrating efficacy in certain patients with acute lymphoblastic leukemia (ALL)

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- - Preliminary study results show 27 of 30 pediatric and adult patients with relapsed/refractory (r/r) ALL (90%) experienced complete remissions with personalized cell therapy, CTL0191
- - Largest published cohort to date for CTL019, which served as the basis for recent Breakthrough Therapy designation from the FDA2
- - Sustained remissions of up to two years in r/r ALL patients with six-month event-free survival of 67% and overall survival of 78%1
- - Novartis and Penn have exclusive global collaboration to research, develop and commercialize CAR T cell therapies for the investigational treatment of cancers

EAST HANOVER, N.J., Oct. 15, 2014 /PRNewswire/ -- Novartis and the University of Pennsylvania's Perelman School of Medicine (Penn) today announced preliminary results from two pilot clinical trials published in The New England Journal of Medicine (NEJM) evaluating the efficacy and safety of CTL019 in patients with relapsed/refractory acute lymphoblastic leukemia (r/r ALL). The studies, conducted by Penn, demonstrated that 27 of 30 pediatric and adult patients, or 90%, experienced complete remissions with the investigational chimeric antigen receptor (CAR) therapy CTL019¹.

"These interim results, which supported the recent FDA Breakthrough Therapy designation, reinforce the potential CTL019 has as a life-saving therapy for patients with relapsed/refractory ALL," said Usman Azam, Global Head, Cell & Gene Therapies Unit, Novartis Pharmaceuticals. "These studies are another promising development in CTL019's history. With each new CTL019 milestone, we are one step closer to potentially offering these seriously ill patients an additional treatment option."

These data build on earlier research findings and are part of two pilot clinical studies that demonstrated sustained remissions of up to two years in pediatric and adult patients with r/r ALL. Median follow-up was just over six months, with event-free survival of 67% and overall survival of 78%. Probability of six-month CTL019 persistence was 68% and CTL019-modified T cells were detectable in the blood by flow cytometry for up to 11 months. Sustained remissions were seen in 15 patients and were associated with CAR T cell persistence and B cell aplasia¹. Updated results have been submitted for presentation at a medical congress taking place later in 2014.

"We are excited by these results, which indicated how effective CTL019 may be in fighting ALL, a leading cause of childhood cancer deaths," said lead investigator Stephan Grupp, MD, PhD, the Yetta Deitch Novotny Professor of Pediatrics in the Perelman School of Medicine at the University of Pennsylvania and director of Translational Research in the Center for Childhood Cancer Research at the Children's Hospital of Philadelphia (CHOP), where 25 pediatric patients were treated in the study cohort¹. "This represents the largest experience to date of CD19-CAR T cells and demonstrates the ability of this approach to achieve sustained complete responses in a patient population with few other treatment options. We are especially hopeful for those patients who remain in remission for 1-2 years without further therapy."

In July 2014, the FDA designated CTL019 as a Breakthrough Therapy under the Penn IND, which is intended to expedite the development and review of drugs that treat serious or life-threatening conditions if the therapy has

demonstrated substantial improvement over an available therapy on at least one clinically significant endpoint³.

Novartis holds the worldwide rights to CARs developed through the collaboration with Penn for all cancer indications, including the lead program, CTL019.

About These Studies

Twenty-five patients enrolled in the pediatric pilot trial at CHOP and 5 patients enrolled in the adult pilot trial at Penn from April 2012 to February 2014. The patients were infused with autologous T cells transduced with a CD19-directed CAR (CTL019) lentiviral vector at doses of 0.7-20.6x10⁶ CTL019 cells/kg. The study found that 27 of 30 pediatric and adult patients with r/r ALL (90%) experienced complete remissions, including two blinatumomab-refractory patients and 15 with prior stem cell transplant¹.

Of the 27 patients who achieved a complete remission, five went off-study for alternate therapy, three of whom proceeded to allogeneic SCT in remission. Fifteen patients remain in remission with a median follow-up of seven months. Sustained remissions were achieved up to two years with six-month event-free survival 67% (95% CI, 51% to 88%) and overall survival 78% (95% CI, 65% to 95%). The probability of six-month CTL019 persistence was 68% (95% CI, 50 to 92%) and relapse-free B cell aplasia was 73% (95% CI, 57 to 97%). CTL019-modified T cells were detectable in the blood by flow cytometry for up to 11 months, and CTL019 sequences remained detectable by quantitative PCR (Q-PCR) in patients with sustained remissions for up to two years¹.

All patients experienced cytokine release syndrome (CRS). Of the 30 patients, 74% (n=22) experienced mild to moderate CRS. Severe CRS, seen in 27% of patients (n=8), was associated with higher disease burden and effectively treated with the IL-6 receptor antibody tocilizumab. Several patients experienced neurologic toxicities, which fully resolved without further intervention or apparent long-term implications¹.

About CTL019

CTL019 uses CAR technology to reprogram a patient's own T cells to "hunt" cancer cells that express specific proteins, called CD19. After they have been reprogrammed, the T cells (now called CTL019) are re-introduced into the patient's blood; they proliferate and bind to the targeted CD19+ cancer cells and destroy them.

Because CTL019 is an investigational therapy, the safety and efficacy profile has not yet been established. Access to investigational therapies is available only through carefully controlled and monitored clinical trials. These trials are designed to better understand the potential benefits and risks of the therapy. Because of uncertainty of clinical trials, there is no guarantee that CTL019 will ever be commercially available anywhere in the world.

About Acute Lymphoblastic Leukemia

Acute lymphoblastic leukemia (ALL) is the most common cancer diagnosed in children, representing approximately 25% of cancer diagnoses among children younger than 15 years, according to data published in 2013⁴. It can also occur in adults. ALL is a type of cancer in which the bone marrow makes too many abnormal white blood cells (lymphocytes). ALL usually gets worse quickly if it is not treated and can be fatal within a few months; therefore, it is critical for patients to start treatment soon after diagnosis. Patients with relapsed ALL experience ALL cells returning in the marrow and a decrease in normal blood cells following their remission. Patients with refractory ALL still have leukemia cells in their bone marrow following treatment⁵.

Disclaimer

The foregoing release contains forward-looking statements that can be identified by words such as "Breakthrough Therapy," "investigational," "potential," "promising," "potentially," "submitted for presentation," "may," "hopeful," "will," or similar terms, or by express or implied discussions regarding potential marketing approvals for CTL019, or regarding potential future revenues from CTL019. You should not place undue reliance on these statements. Such forward-looking statements are based on the current beliefs and expectations of management regarding

future events, and are subject to significant known and unknown risks and uncertainties. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those set forth in the forward-looking statements. There can be no guarantee that CTL019 will be submitted or approved for sale in any market, or at any particular time. Nor can there be any guarantee that CTL019 will be commercially successful in the future. In particular, management's expectations regarding CTL019 could be affected by, among other things, the uncertainties inherent in research and development, including unexpected clinical trial results and additional analysis of existing clinical data; unexpected regulatory actions or delays or government regulation generally; the company's ability to obtain or maintain proprietary intellectual property protection; general economic and industry conditions; global trends toward health care cost containment, including ongoing pricing pressures; unexpected manufacturing issues, and other risks and factors referred to in Novartis AG's current Form 20-F on file with the US Securities and Exchange Commission. Novartis is providing the information in this press release as of this date and does not undertake any obligation to update any forward-looking statements contained in this press release as a result of new information, future events or otherwise.

About Novartis

Novartis Pharmaceuticals Corporation researches, develops, manufactures and markets innovative prescription drugs used to treat a number of diseases and conditions, including cardiovascular, dermatological, central nervous system, bone disease, cancer, organ transplantation, psychiatry, infectious disease and respiratory. The company's mission is to improve people's lives by pioneering novel healthcare solutions.

Located in East Hanover, New Jersey, Novartis Pharmaceuticals Corporation is an affiliate of Novartis AG, which 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, eye care, cost-saving generic pharmaceuticals, preventive vaccines, over-the-counter and animal health products. Novartis is the only global company with leading positions in these areas. In 2013, the Group achieved net sales of USD 57.9 billion, while R&D throughout the Group amounted to approximately USD 9.9 billion (USD 9.6 billion excluding impairment and amortization charges). Novartis Group companies employ approximately 135,000 full-time-equivalent associates and sell products in more than 150 countries around the world. For more information, please visit <http://www.novartis.com>.

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