NOVARTIS

Novartis pivotal CTL019 6-month follow-up data show durable remission rates in children, young adults with r/r B-cell ALL

Jun 23, 2017

- - 83% of patients achieved complete remission (CR) or CR with incomplete blood count recovery within 3 months of treatment with CTL019; consistent with interim ELIANA data
- - Data evaluating 63 patients demonstrate relapse-free survival and probability of survival in a majority of patients at six months
- - Advances in CTL019 and ELIANA result from global CAR-T cell therapy collaboration with the University of Pennsylvania
- - CTL019 is manufactured using cryopreserved leukapheresis which, in the ELIANA trial, enabled the treatment of patients in 25 sites across four continents

EAST HANOVER, N.J., June 23, 2017 /PRNewswire/ -- Novartis today announced updated results from the ELIANA clinical trial demonstrating CTL019 (tisagenlecleucel) remission rates are maintained at six months in relapsed/refractory (r/r) pediatric and young adult patients with B-cell acute lymphoblastic leukemia (ALL). These data from this pivotal trial of CTL019 show that 83% (52 of 63; 95% confidence interval [CI]: 71%-91%) of patients achieved complete remission (CR) or CR with incomplete blood count recovery within three months of infusion. No minimal residual disease (MRD) was detected among responding patients[1]. MRD, which measures the elimination of residual disease in the blood and bone marrow at the molecular level following treatment, is important because it may be an indicator of potential relapse[2]. Results from this study of CTL019 – an investigational chimeric antigen receptor T cell (CAR-T) therapy – will be presented at the European Hematology Association (EHA) Annual Meeting (Abstract #S476; Saturday, June 24, 4:00 PM CEST).

The ELIANA study also showed that the relapse-free probability was 75% (95% CI, 57%-87%; median duration of response not reached) at six months and 64% (95% CI, 42%-79%) at 12 months among responders. In addition, the probability of survival was 89% (95% CI, 77%-94%) at six months and 79% (95% CI, 63%-89%) at 12 months. The median time from infusion to data cutoff was 8.8 months[1].

"The updated CTL019 ELIANA data illustrating early observed response rates that have held steady over six months' time are exciting findings. Durability is an important measure for children and young adults with relapsed or refractory B-cell ALL, and we are truly encouraged by the results of this study," said lead investigator Stephan Grupp, MD, PhD, the Yetta Deitch Novotny Professor of Pediatrics at the Perelman School of Medicine at the University of Pennsylvania (Penn), and Director of the Cancer Immunotherapy Frontier Program at the Children's Hospital of Philadelphia (CHOP).

Forty-seven percent of patients in ELIANA experienced grade 3 or 4 cytokine release syndrome (CRS), a known complication of the investigational therapy that may occur when the engineered cells become activated in the patient's body. CRS was managed globally using prior site education on implementation of the CRS treatment algorithm. There were no deaths due to refractory CRS and no incidents of cerebral edema were reported. Fifteen percent of patients experienced grade 3 neurologic events, with no grade 4 events seen[1].

The ELIANA trial enrolled 88 patients. Of the 88, 16 patients discontinued before infusion and the majority (nine patients) did so due to rapid progression of their disease or deterioration in their clinical status. This reflects the acute and progressive nature of this disease. Of the 16 patients who weren't infused, seven were a result of insufficiently formulated CAR-T cell product. Additionally, five infused patients had not reached three-month follow-up and four patients were pending infusion at the time of data cutoff.

"These positive, updated ELIANA data help us better understand the ability for CTL019 to maintain durable responses in r/r ALL," said Vas Narasimhan, MD, Global Head of Drug Development and Chief Medical Officer, Novartis. "The results, including relapse-free survival findings at six and 12 months, reaffirm our confidence in CTL019 to potentially become an effective treatment for pediatric and young adult patients with r/r ALL in need of more options."

ELIANA (NCT02435849) is the first pediatric global CAR-T cell therapy registration trial, with study enrollment having occurred across 25 centers in the US, Canada, EU, Australia and Japan. The single-arm, open-label, multicenter Phase II study included patients aged three to 23 years who were primary refractory, refractory to chemotherapy after their first relapse, relapsed after second line therapy or ineligible for an allogeneic stem cell transplant (SCT). Patients in the trial received a median of three prior lines of therapy and 59% of patients had a prior SCT.

CTL019 was first developed by Penn and uses the 4-1BB costimulatory domain to enhance cellular responses. In 2012, Novartis and Penn entered into a global collaboration to further research, develop and then commercialize CAR-T cell therapies, including CTL019, for the investigational treatment of cancers.

Additional CTL019 data at EHA

A pooled data analysis from two multicenter trials of CTL019 in pediatric and young adult patients with r/r B-cell ALL, including ELIANA and ENSIGN (NCT02228096), will also be highlighted in a presentation at the meeting. This research is aimed to identify any new safety issues with CTL019 as a result of its use in multicenter trials, which included 25 sites across 11 countries. Study authors concluded that there were no new safety issues and that CRS and neurologic events were effectively managed. Prolonged follow-up will be required to determine the long-term safety of B-cell aplasia (Abstract #P517; Saturday, June 24, 5:30 PM CEST).

An oral presentation will feature pooled analyses from two multicenter trials of CTL019 in pediatric and young adult patients with r/r B-cell ALL, including ELIANA and ENSIGN, observing response analysis and impact of intrinsic/extrinsic and manufacturing factors on CTL019 expansion and persistence (Abstract #S477; Saturday, June 24, 4:15 PM CEST).

Novartis will also present an encore of results from its global, pivotal multi-center Phase II JULIET study (NCT02445248; Abstract #LB2604, June 25, 12:00 PM CEST), evaluating CTL019 in adults with r/r diffuse large-b-cell lymphoma (DLBCL).

CTL019 was granted Priority Review from the FDA earlier this year in the treatment of r/r pediatric and young adult patients with B-cell ALL, and Novartis plans to file with the European Medicines Agency (EMA) later in 2017. The investigational therapy received PRIME (PRIority MEdicines) designation from the EMA in 2016. The FDA also granted Breakthrough Therapy designation to CTL019 for the treatment of adult patients with r/r DLBCL, whose disease has progressed on or after two or more prior therapies.

About CTL019 Manufacturing

Novartis leukapheresis process using cryopreservation allowed for manufacturing and treatment of patients from around the world. Cryopreserved leukapheresis gives physicians the flexibility to schedule apheresis at a time that is in the best interest of their patients. Novartis commercial manufacturing for CTL019 continues to

build on its experience in its Morris Plains, New Jersey facility, which has already manufactured CTL019 for hundreds of patients in global clinical trials. Novartis believes that experience is important in cell therapy manufacturing, and the experience gained at the Morris Plains, New Jersey facility will be a foundation for commercial manufacturing of CAR-T therapies. Novartis has made and continues to make investments in manufacturing.

About CAR-T and CTL019

CAR-T 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 hunt the patient's cancer cells and other B-cells expressing a particular antigen. In March 2017, Novartis announced that the FDA granted Priority Review for the company's Biologics License Application for CTL019 in the treatment of r/r pediatric and young adult patients with B-cell ALL.

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 the uncertainty of clinical trials, there is no guarantee that CTL019 will ever be commercially available anywhere in the world.

About ALL

Acute lymphoblastic leukemia makes up approximately 25% of cancer diagnoses among children under 15 years old and is the most common childhood cancer in the US[3]. Patients with r/r ALL have limited treatment options, and the chance of survival for children with the disease who relapse or fail to attain remission is between 16% to 30.1%[4].

Disclaimer

The foregoing release contains forward-looking statements that can be identified by words such as "investigational," "will," "exciting," "encouraged," "confidence," "potentially," "aimed," "Priority Review," "plans," "later in 2017," "PRIME designation," "Breakthrough Therapy designation," "to build," "believes," "continues," "yet," 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 clinical trial results and additional analysis of existing clinical data; 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 and reimbursement pressures; safety, quality or 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

Located in East Hanover, NJ Novartis Pharmaceuticals Corporation is an affiliate of Novartis 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, cost-saving generic and biosimilar pharmaceuticals and eye care. Novartis has leading positions globally in each of these areas. In 2016, the Group achieved net sales of USD 48.5 billion, while R&D throughout the Group amounted to approximately USD 9.0 billion. Novartis Group companies employ approximately 118,000 full-time-equivalent associates. Novartis products are sold in approximately 155 countries around the world. For more information, please visit http://www.novartis.com.

Novartis is on Twitter. Sign up to follow @Novartis at http://twitter.com/novartis and @Novartis Cancer at http://twitter.com/novartiscancer.

For Novartis multimedia content, please visit www.novartis.com/news/media-library

For questions about the site or required registration, please contact media.relations@novartis.com

References

1. Buechner, Jochen Et Al. Global Registration Trial Of Efficacy And Safety Of Ctl019 In Pediatric And Young Adult Patients With Relapsed/Refractory (R/R) Acute Lymphoblastic Leukemia (All): Update To The Interim Analysis. June 24, 4:00 Pm CEST. European Hematology Association: Abstract S476.
2. Campana, Dario. Minimal Residual Disease in Acute Lymphoblastic Leukemia. Seminars in hematology 46.1 (2009): 100–106. PMC. Web. 22 May 2017.
3. Howlader, N., Noone, A. M., Krapcho, M, et al. SEER Cancer Statistics Review, 1975–2010. National Cancer Institute, April 2013; Section 28.9 (12). http://www.seer.cancer.gov/csr/1975_2010/results_merged/sect_28_childhood_cancer.pdf. Accessed June 2017.
4. Satwani, Prkash, Sather, Harland, Ozkaynak, Fevzi, et al. Allogeneic Bone Marrow Transplantation in First Remission for Children with Ultra-high-risk Features of Acute Lymphoblastic Leukemia: A Children's Oncology Group Study Report." Biology of Blood and Marrow Transplantation 13.2 (2007): 218-27. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2731715/. Accessed June 2017.

Novartis Media Relations
Central media line: +41 61 324 2200
E-mail: media.relations@novartis.com

Eric Althoff	Fiona Phillips
Novartis Global Media Relations	Novartis Oncology Communications
+41 61 324 7999 (direct)	+1 862-778-7705 (direct)
+41 79 593 4202 (mobile)	+1 862-217-9396 (mobile)
eric.althoff@novartis.com	fiona.phillips@novartis.com

SOURCE Novartis

show-durable-remission-rates-children-young-adults-rr-b-cell-all

List of links present in page

1. https://qa1.novartis.us/us-en/us-en/news/media-releases/novartis-pivotal-ctl019-6-month-follow-data-show-durable-remission-rates-children-young-adults-rr-b-cell-all
2. http://www.novartis.com/
3. http://twitter.com/novartis
4. http://twitter.com/novartiscancer
5. http://www.novartis.com/news/media-library
6. mailto:media.relations@novartis.com
7. http://www.seer.cancer.gov/csr/1975_2010/results_merged/sect_28_childhood_cancer.pdf
8. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2731715/
9. mailto:media.relations@novartis.com
10. mailto:eric.althoff@novartis.com
11. mailto:fiona.phillips@novartis.com