NOVARTIS

Novartis drug crizanlizumab shown to prolong time to patients' first sickle cell pain crisis in subgroup analysis of SUSTAIN study

Dec 11, 2017

- - Investigational therapy crizanlizumab (SEG101, formerly SelG1) approximately doubled the time to first on-treatment sickle cell pain crisis, according to new subgroup analysis of Phase II SUSTAIN data
- - Results were consistent across patient subgroups despite differences in disease severity, genotype or background therapy
- - New findings for crizanlizumab, a potential disease-modifying, preventive treatment option for patients with sickle cell disease, presented at ASH 2017
- - Discussions with health authorities continue; FDA filing anticipated by end of 2018 pending outcome of ongoing healthy volunteer bridging study

EAST HANOVER, N.J., Dec. 11, 2017 /PRNewswire/ -- Results from a post hoc subgroup analysis of the Phase II SUSTAIN study show that crizanlizumab, an investigational humanized anti-P-selectin monoclonal antibody, delayed the time to first sickle cell pain crisis (SCPC) in patients vs. placebo in key subgroups of adult patients with sickle cell disease[1]. Findings were featured during an oral session at the 59th American Society of Hematology (ASH) Annual Meeting (Abstract #613; Monday, December 11, 10:30 AM ET).

Acute sickle cell pain crises, also referred to as vaso-occlusive crises, are a common painful complication of the disease and the main reason that patients seek medical care in hospitals.[2] Currently, treatment options are limited. The data from a subgroup analysis of the Phase II SUSTAIN study showed that crizanlizumab, at 5.0 mg/kg per month increased the time to SCPC in patients on treatment, including those in high-risk subpopulations and with hydroxyurea use[1].

"Pain is the primary cause of suffering in sickle cell disease," said Julie Kanter, M.D., Division of Pediatrics, Medical University of South Carolina, a study investigator. "What this new analysis of the SUSTAIN data suggests is that once patients start crizanlizumab, they are likely to have a longer time before experiencing another pain crisis. These findings are consistent regardless of the severity of disease, genotype, or the use of background therapy. That is a potentially promising new development for patients. Fewer pain crises mean less organ damage long term."

The analysis looked at the following subgroups of patients with sickle cell disease:

- Patients with 2-4 or 5-10 SCPC events in the year before the study
- Patients with the HbSS genotype, and non-HbSS genotypes
- Patients who were or were not taking hydroxyurea

In all of these subpopulations, crizanlizumab at 5.0 mg/kg per month increased the estimated median time to first SCPC vs. placebo by approximately two-fold or more.

In patients taking crizanlizumab who experienced 2-4 SCPCs in the prior year, time to first on-treatment pain crisis was 4.8 vs 1.6 months with placebo (HR 0.53 with 95% CI [0.31, 0.90]). For patients with 5-10 SCPCs in

the prior year, time to first on-treatment pain crisis was 2.4 vs 1.0 months (HR 0.47 with a 95% CI [0.25, 0.89]).

In patients with the HbSS genotype, there was a 3.7-fold increase in estimated median time to first SCPC in those taking crizanlizumab vs. placebo (4.1 vs 1.1 months; HR 0.50 with 95% CI [0.31, 0.80]). In patients taking hydroxyurea, the time to first on-study SCPC was longer with crizanlizumab vs placebo (2.4 vs 1.2 months; HR 0.58 with 95% CI [0.35, 0.96]), suggesting its potential as an additive therapy[1].

"This analysis from SUSTAIN is another important step to bringing what we hope will be a new disease-modifying therapy to patients with sickle cell disease," said Samit Hirawat, MD, Head, Novartis Oncology Global Drug Development. "The results are consistent among different groups of patients, which gives us even more confidence in our development program for this promising medicine."

About the Subgroup Analysis and the SUSTAIN trial

The heterogeneity in severity of sickle cell disease and various other factors make it important to understand differences in response of various subgroups of patients in order to increase understanding of crizanlizumab and the role of P-selectin in SCD. This post hoc analysis evaluated the time to first SCPC among subgroups of the SUSTAIN study population – those who had 2-4 or 5-10 SCPCs within the prior year; patients with HbSS or non-HbSS genotypes; and patients with or without concomitant treatment with hydroxyurea. The goal was to further assess the efficacy of crizanlizumab at 5.0 mg/kg per month vs placebo, and identify differences in treatment response among those subgroups[1].

The SUSTAIN trial was a multicenter, multinational, randomized, placebo-controlled, double-blind, 12-month study to assess safety and efficacy of the anti-P-selectin antibody crizanlizumab with or without concomitant use of hydroxyurea therapy in sickle cell disease patients with sickle cell-related pain crises. Results, which were published in The New England Journal of Medicine, showed that crizanlizumab reduced the median annual rate of SCPCs by 45% compared to placebo (1.6 vs 3.0, p=0.01) in patients with or without hydroxyurea therapy.[3] These data will help support discussions with regulatory agencies, with filing anticipated in the U.S. by the end of 2018.

Adverse events that occurred in 10% or more of the patients in either active-treatment group and at a frequency that was at least twice as high as that in the placebo group were arthralgia, diarrhea, pruritus, vomiting, and chest pain. There were no apparent increases in infections with crizanlizumab treatment.[3]

About crizanlizumab (SEG101)

Crizanlizumab (SEG101) is an investigational humanized anti-P-selectin monoclonal antibody that binds a molecule called P-selectin on the surface of endothelial cells and platelets in the blood vessels, causing a blockade of P-selectin[3,4]. P-selectin is a driver of the vaso-occlusive process[3,5]. Vaso-occlusive crises, also known as SCPCs, occur episodically when sickle-shaped red blood cells block blood flow through blood vessels[6]. The therapeutic blockade of P-selectin can prevent painful vaso-occlusion in small blood vessels and maintain blood flow[3,6].

Disclaimer

This press release contains forward-looking statements within the meaning of the United States Private Securities Litigation Reform Act of 1995. Forward-looking statements can generally be identified by words such as "potential," "can," "will," "plan," "expect," "anticipate," "look forward," "believe," "committed," "investigational," "pipeline," "launch," or similar terms, or by express or implied discussions regarding potential marketing approvals, new indications or labeling for the investigational or approved products described in this press release, or regarding potential future revenues from such products. You should not place undue reliance on these statements. Such forward-looking statements are based on our current beliefs and expectations

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 the investigational or approved products described in this press release will be submitted or approved for sale or for any additional indications or labeling in any market, or at any particular time. Nor can there be any guarantee that such products will be commercially successful in the future. In particular, our expectations regarding such products 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; our ability to obtain or maintain proprietary intellectual property protection; the particular prescribing preferences of physicians and patients; global trends toward health care cost containment, including government, payer and general public pricing and reimbursement pressures; general economic and industry conditions, including the effects of the persistently weak economic and financial environment in many countries; 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 @NovartisCancer at https://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. Kanter J, Kutlar A, Liles D, et al. Crizanlizumab 5.0 mg/kg increased the time to first on-treatment sickle cell pain crisis: A subgroup analysis of the Phase II SUSTAIN study. Abstract #613. 2017 59th American Society of Hematology (ASH) Annual Meeting, Atlanta, GA.
2. Puri L, Nottage K et al. State of the Art Management of Acute Vaso-occlusive Pain in Sickle Cell Disease Pediatr Drugs, epub Aug 2017 DOI 10.1007/s40272-017-0263-z
3. Ataga KI, Kutlar A, Kanter J et al. Crizanlizumab for the Prevention of Pain Crises in Sickle Cell Disease. N Engl J Med. 2017 Feb 2;376(5):429-439.
4. Miller ST, Kim HY, et al. for Sickle Cell Disease Clinical Research Network (SCDCRN). Inpatient management of sickle cell pain: A 'snapshot' of current practice. Am J Hematol. 2012 Mar;87(3):333–336.
5. Novartis Pharmaceuticals Corporation. Data on file. 2016.
6. Quinn CT. Anti-adhesive therapy for sickle cell disease. The Hematologist. 2014; 11(6):15.

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

Eric Althoff	Michael Billings
Novartis Global Media Relations	Novartis Oncology Communications
+41 61 324 7999 (direct)	+1 862 778 8656 (direct)
+41 79 593 4202 (mobile)	+1 201 400 1854 (mobile)
eric.althoff@novartis.com	michael.billings@novartis.com

SOURCE Novartis Pharmaceuticals Corporation

Source URL: *https://qa1.novartis.us/us-en/news/media-releases/novartis-drug-crizanlizumab-shown-prolong-time-patients-first-sickle-cell-pain-crisis-subgroup-analysis-sustain-study*

List of links present in page

1. https://qa1.novartis.us/us-en/us-en/news/media-releases/novartis-drug-crizanlizumab-shown-prolong-time-patients-first-sickle-cell-pain-crisis-subgroup-analysis-sustain-study
2. http://www.novartis.com/
3. http://twitter.com/novartis
4. https://twitter.com/novartiscancer
5. http://www.novartis.com/news/media-library
6. mailto:media.relations@novartis.com
7. mailto:media.relations@novartis.com
8. mailto:eric.althoff@novartis.com
9. mailto:michael.billings@novartis.com