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Novartis analysis shows crizanlizumab (SEG101) increased the number of patients free of sickle cell pain crises vs placebo during SUSTAIN study

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- - Data published in the American Journal of Hematology show more than twice as many patients taking crizanlizumab did not experience a disease-related pain crisis (also called vaso-occlusive crisis, or VOC) vs placebo
- - VOCs are the most common, painful complication of sickle cell disease and the main reason patients seek medical care in hospitals
- - Discussions with health authorities continue; FDA filing anticipated in 2019

EAST HANOVER, N.J., Oct. 9, 2018 /PRNewswire/ -- Results from a post hoc analysis of the Phase II SUSTAIN study of crizanlizumab, a humanized anti-P-selectin monoclonal antibody being investigated for the treatment of sickle cell disease (SCD), have been published in the American Journal of Hematology. The analysis showed that more patients treated with crizanlizumab did not experience a vaso-occlusive crisis (VOC) vs those treated with placebo (35.8% vs 16.9%), specifically patients with a history of 2-10 VOCs in the previous year.

VOCs are a painful complication of SCD and the main reason why patients seek medical care in hospitals[1,2]. VOCs, which are triggered by multi-cell adhesion, are associated with increased morbidity and mortality, and can result in stroke, as well as organ damage or failure[3,4]. Currently, treatment options for VOCs are limited[5].

"The unpredictable, intense painful crises that patients with sickle cell disease experience are the hallmark of the disease and the primary cause of hospitalizations in this patient population," said Abdullah Kutlar, MD, Director, Sickle Cell Center at the Medical College of Georgia, Augusta University, Augusta, Georgia, and primary author of the SUSTAIN analysis. "I am encouraged that results from this post hoc analysis of SUSTAIN study data found that crizanlizumab could substantially delay or prevent these crises, which also may mean less organ damage in the long run."

The post hoc analysis reviewed 52-week results from 132 patients, including 67 treated with crizanlizumab 5 mg/kg and 65 who received placebo. All evaluated patients had a history of at least 2 VOCs in the year prior to the study, with 62.9% (n=83) having experienced 2-4 events and 37.1% (n=49) with 5-10 events. The most common genotype in SCD, homozygous hemoglobin S (HbSS), was identified in most SUSTAIN patients (n=94; 71.2%), and patients with this genotype were evenly distributed between study arms.

The analysis found that treatment with crizanlizumab may prevent VOCs, both in patients who had 2-4 and 5-10 disease-related pain events in the year prior to the study, as well as those with HbSS.

Of the subgroups evaluated, a considerable number of patients across multiple subgroups treated with crizanlizumab did not experience a VOC compared with those treated with placebo, including:

- Those with 2-4 events in the year prior to participating in the study (17 out of 42 patients or 40.5% vs 10 out of 41 patients, or 24.4%)

- Those with 5-10 events in the year prior to participating in the study (7 out of 25 patients or 28.0% vs 1 out of 24 patients, or 4.2%)
- Those with the HbSS genotype (15 out of 47 patients or 31.9% vs 8 out of 47 patients, or 17.0%)
- Those also with concomitant use of hydroxyurea (14 out of 42 patients 33.3% vs 7 out of 40 patients, or 17.5%)

No new safety concerns emerged in the post hoc analysis as adverse events attributed to treatment were similar between the crizanlizumab and placebo arms across all subgroups.

"The insights gained from this analysis and others from the SUSTAIN study, strengthen our belief that crizanlizumab may become an important new therapeutic option for sickle cell patients who continue to need step changes in medical innovation," said Samit Hirawat, MD, Head, Novartis Oncology Global Drug Development. "This is another example of what we mean when we say we are reimagining medicine."

About the SUSTAIN trial

The Phase II 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. Primary results were published in The New England Journal of Medicine and showed that crizanlizumab reduced the median annual rate of sickle cell pain crises (SCPCs) by 45.3% compared to placebo (1.63 vs 2.98, p=0.010) in patients with or without hydroxyurea therapy[6].

Adverse events that occurred in 10% or more of the patients in either active-treatment group (2.5 mg/kg; 5 mg/kg) 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[6].

About crizanlizumab (SEG101)

Crizanlizumab (SEG101) is a humanized anti-P-selectin monoclonal antibody being investigated for the prevention of vaso-occlusive crises (VOCs) in patients with sickle cell disease (SCD)[6]. Crizanlizumab binds a molecule called P-selectin on the surface of endothelial cells and platelets in the blood vessels, causing a blockade of P-selectin[6]. P-selectin is one of the major drivers of the vaso-occlusive process[6]. Results from the Phase II SUSTAIN study demonstrated that crizanlizumab reduced the median annual rate of VOCs that lead to a healthcare visit compared to placebo in patients with SCD regardless of whether or not they were taking hydroxyurea[6].

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