Novartis announces new crizanlizumab (SEG101) data analysis in sickle cell disease, and investment in SENTRY clinical program

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- -New post-hoc analysis of SUSTAIN study, presented at ASH 2018, highlights results among patients who were treated per protocol compared with all randomized patients
- -Crizanlizumab, a monthly infusion being investigated for the treatment of sickle cell disease, approximately halved the annual rate of sickle cell disease-related pain crises (also called vaso-occlusive crises, or VOCs) vs placebo
- -SENTRY is an umbrella clinical trial program comprising initially seven active or planned trials of crizanlizumab in sickle cell disease; more trials may be added

EAST HANOVER, N.J., Dec. 1, 2018 /PRNewswire/ -- New data from a post hoc analysis of the Phase II SUSTAIN study of crizanlizumab -- a once-a-month, humanized anti-P-selectin monoclonal antibody infusion being investigated for the treatment of sickle cell disease (SCD) -- shows greater reductions of vaso-occlusive crises (VOCs) in patients who were adherent to the treatment protocol. The data were presented during the 60th Annual Meeting of the American Society of Hematology (ASH) in San Diego.

Sickle cell VOCs are painful complications of the disease and the main reason why patients seek medical care in hospitals[1,2]. These crises are triggered by multi-cell adhesion, or clusters of cells that block blood flow, and are associated with increased morbidity and mortality[3,4]. Currently, treatment options to prevent VOCs are limited. By targeting P-selectin, crizanlizumab reduces multicellular adhesion[2,5].

"Patients with sickle cell disease experience recurrent and severe episodes of debilitating pain that often require medical attention and emergency medical care," said Kenneth Ataga, MD, Director of the Center for Sickle Cell Disease at the University of Tennessee Health Science Center at Memphis, and Principal Investigator of the SUSTAIN analysis. "It is encouraging that these data show treatment per protocol not only reduced the frequency of painful crises, but also increased the number patients with no crises at all. These findings underscore the potential of crizanlizumab and the importance of proactive management of sickle cell disease."

In the analysis of the per protocol population of the 52-week SUSTAIN study, which compared the P-selectin inhibitor crizanlizumab with placebo in patients with sickle cell disease, crizanlizumab (5.0 mg/kg) significantly:

- Increased the percentage of patients who did not experience any VOCs vs placebo (37.5% vs. 12.2%, p=0.008) during treatment
- More than doubled the median time to first on-treatment VOC (6.55 vs 1.58 months, $p < 0.001$) and
- Decreased the annual rate of VOCs (1.04 vs 2.18, p=0.02).

SUSTAIN is part of the SENTRY clinical trial program including seven active or planned clinical studies designed to generate an array of additional data on the role crizanlizumab plays in the management of sickle cell disease. More studies may be added as plans are finalized.

Major active trials in the SENTRY program include:

- SOLACE-adults (A2202) Phase II study investigating the pharmacological properties and safety of crizanlizumab in patients with sickle cell disease aged 16 and above
- SOLACE-kids (B2201) Phase II study investigating the safety and efficacy of crizanlizumab in pediatric patients with sickle cell disease
- STAND (A2301) Phase III study investigating the efficacy and safety of crizanlizumab in sickle cell disease patients aged 12 and above
- SUCCESSOR retrospective cohort study among adult sickle cell disease patients in the US

"The SENTRY program emphasizes our long-term commitment to reimagining sickle cell disease treatment for as many people as possible," said Samit Hirawat, MD, Head, Novartis Oncology Global Drug Development. "The outcomes of these trials, alongside our analyses of SUSTAIN, will increase our understanding of the disease and, we hope, take us a step forward in our aspiration to reduce the burden of sickle cell pain crises."

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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