Novartis investigational therapy crizanlizumab (SEG101) receives FDA Breakthrough Therapy designation for the prevention of vaso-occlusive crises in sickle cell disease

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- - Crizanlizumab is a monthly infusion under development to prevent pain crises (also called vaso-occlusive crises, or VOCs) in patients with sickle cell disease
- - Sickle cell VOCs, which are triggered by multi-cell adhesion or clusters of cells that block or reduce blood flow, are associated with increased morbidity and mortality(1)
- - FDA filing of crizanlizumab anticipated in first half of 2019

BASEL, Switzerland, Jan. 8, 2019 /PRNewswire/ -- Novartis announced today that the US Food and Drug Administration (FDA) has granted crizanlizumab (SEG101) Breakthrough Therapy designation for the prevention of vaso-occlusive crises (VOCs) in patients of all genotypes with sickle cell disease (SCD). Also known as sickle cell pain crises, VOCs are unpredictable and extremely painful events that can lead to serious acute and chronic complications[2]. VOCs happen when multiple blood cells stick to each other and to blood vessels, causing blockages[1,3]. Treatments that make blood cells and blood vessels less sticky may help reduce the number of days patients experience VOCs.

"Painful sickle cell crises matter because they can disrupt patients' lives, and often require hospital visits and medical attention," said Samit Hirawat, MD, Head, Novartis Oncology Global Drug Development. "We look forward to working closely with the FDA over the coming months toward making crizanlizumab, a therapy that has the potential to prevent sickle cell pain crises, available in the US as soon as possible."

According to FDA guidelines, treatments that receive Breakthrough Therapy designation are those that treat a serious or life-threatening disease or condition and demonstrate a substantial improvement over existing therapies on one or more significant end points based on preliminary clinical evidence.

The FDA granted Breakthrough Therapy designation for crizanlizumab based on positive results of the Phase II SUSTAIN trial, which compared the P-selectin inhibitor crizanlizumab with placebo in patients with sickle cell disease. SUSTAIN showed that crizanlizumab reduced the median annual rate of VOCs leading to health care visits by 45.3% compared to placebo (1.63 vs 2.98, P=0.010) in patients with or without hydroxyurea therapy. The study also demonstrated that crizanlizumab significantly increased the percentage of patients who did not experience any VOCs vs placebo (35.8% vs 16.9%, P=0.010) during treatment[4].

Patients taking crizanlizumab (5 mg/kg) experienced a similar incidence of treatment-emergent adverse events (AEs) (86.4% vs 88.7%) and serious AEs (25.8% vs 27.4%) compared to placebo, and a low incidence of discontinuations (3%) due to adverse events. 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 included arthralgia, diarrhea, pruritus, vomiting, and chest pain. There were no apparent increases in infections with crizanlizumab treatment[4].

About Sickle Cell Disease (SCD)

Sickle cell disease is a debilitating genetic blood disorder that affects the shape of your red blood cells and can make blood cells and blood vessels stickier than usual[1,5]. When blood cells stick to one another they can form clusters in the bloodstream. These clusters can block the flow of blood and oxygen, which can cause damage to the blood vessels and organs[1,3]. These blockages also can lead to painful crises called vaso-occlusive crises, or VOCs. VOCs are painful complications of the disease and the main reason why patients seek medical care in hospitals[1]. Treatment of sickle cell disease is also associated with a high economic burden. The average sickle cell disease patient is estimated to face nearly $1 million in total lifetime health care costs with annual costs of more than $30,000 for adults[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). Crizanlizumab binds to a molecule called P-selectin on the surface of platelets and endothelium in the blood vessels and has been shown to inhibit interactions between endothelial cells, platelets, red blood cells, sickled red blood cells, and leukocytes, causing a blockade and thereby preventing these cells from being able to bind to P-selectin. P-selectin is one of the major drivers of the vaso-occlusive process. Our goal is to deepen understanding of the true impact of VOCs on patients' bodies and lives and to explore how crizanlizumab can help to achieve more pain-crisis-free days for patients with SCD[4].

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References

1. Gutsaeva D, Parkerson J, Yerigenahally S, et. Inhibition of cell adhesion by anti–P-selectin aptamer: a new potential therapeutic agent for sickle cell disease. Blood. 2011;117(2):727-735.

2. Yale SH. Approach to the vaso-occlusive crisis in adults with sickle cell. Am Fam Physician. 2000 Mar 1;61(5):1349-1356.

3. Steinberg M. Management of sickle cell disease. N Engl J Med. 1999;340(13):1021-1030.

4. Ataga KI, Kutlar A, Kanter J et al. Crizanlizumab for the prevention of pain crises in sickle cell disease. N Engl J Med. 2017. 376(5):429-439.

5. Sparkenbaugh E, Pawlinski R. Interplay between coagulation and vascular inflammation in sickle cell disease. J Haematol. 2013;162(1):1-22.

6. American Society of Hematology. State of sickle cell disease 2016 report. Available from: http://www.scdcoalition.org/pdfs/ASH%20State%20of%20Sickle%20Cell%20Dis…. Accessed on July 17, 2018.

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