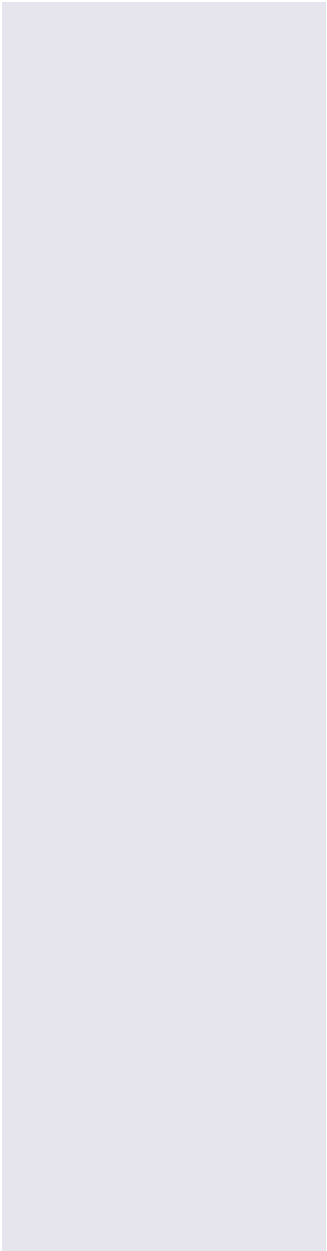




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Sickle cell pain crises are the most common cause of emergency room visits and hospitalizations resulting in decreased quality of life and increased risk of death. They are variable in frequency, duration, and severity making them unpredictable and sometimes unbearable. Pain crises are the result of a complex interaction between blood cells including sickle red blood cells that carry oxygen, white blood cells that fight infection and are important in inflammation, platelets that cause blood to clot, and the lining of the blood vessels known as endothelium. P-selectin acts as a glue-like molecule causing sickle cells and white blood cells to stick to the vascular endothelium and also causing platelets to stick to the red cells and white cells. The adhesion of cells to vascular endothelium and to other cells creates blockages of blood flow known as vaso-occlusion. This process deprives the tissues of oxygen resulting in ischemia, multiorgan dysfunction, and pain. Now there is new hope for prevention of pain crises with a novel drug called crizanlizumab.

Crizanlizumab (SelG1 developed by Selexys Pharmaceuticals and acquired by Novartis Pharmaceuticals) is a humanized monoclonal antibody that blocks binding to P-selectin and the complex interactions described above. Results from the Phase 2 SUSTAIN clinical trial demonstrated that crizanlizumab prevents pain crises. The multicenter study enrolled 198 patients aged 16-65 years with all the common sickle cell genotypes (hemoglobin SS, SC, S⁰ thalassemia, and S⁺ thalassemia) who had 2-10 pain crises per year at baseline. Patients were randomized into three arms. High-dose crizanlizumab (5 mg/kg) was given to 67 patients, 66 patients received low-

dose crizanlizumab (2.5 mg/kg), while 65 patients received placebo without drug. Patients received two loading doses given intravenously (IV) two weeks apart followed by IV infusion of doses every 4 weeks for one year. The primary outcome was the annual rate of pain crises also evaluating episodes of acute chest syndrome, hepatic and splenic sequestration, and priapism. Secondary endpoints included annual rate of days hospitalized, time to first and second pain crisis, and markers of hemolysis including hemoglobin, lactate dehydrogenase., and haptoglobin. The primary outcome was the annual rate of pain crises also evaluating episodes of acute chest syndrome, hepatic and splenic sequestration, and priapism. Secondary endpoints included annual rate of days hospitalized, time to first and second pain crisis, and markers of hemolysis including hemoglobin, lactate dehydrogenase., and haptoglobin. The primary outcome was the annual rate of pain crises also evaluating episodes of acute chest syndrome, hepatic and splenic sequestration, and priapism. Secondary endpoints included annual rate of days hospitalized, time to first and second pain crisis, and markers of hemolysis including hemoglobin, lactate dehydrogenase., and haptoglobin.

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The Big Surprise: Part II

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