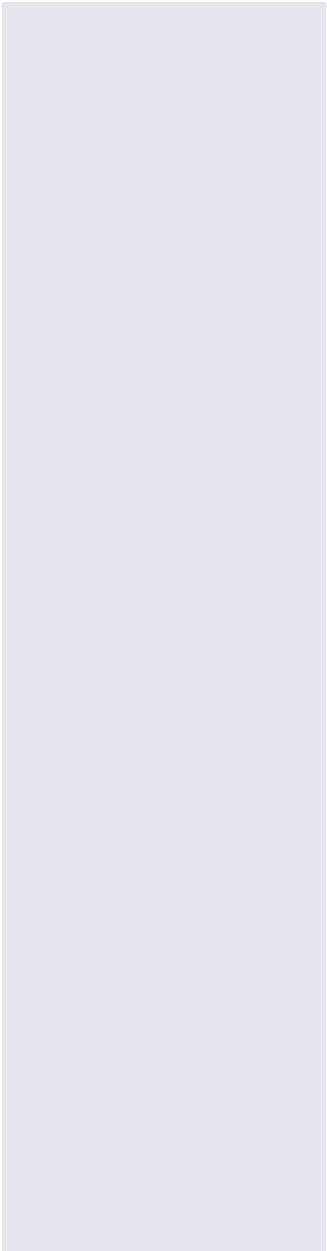




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Sickle cell pain crises are the most common cause of emergency room visits and hospitalizations resulting in decreased quality of life and increased risk of death. They are variable in frequency, duration, and severity making them unpredictable and 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., andlil2(ernliz(ain c(aipF10 yaipFu(erli1cer y)2266 p)9rooi (a) Secondarcome was (s b (enousTJT]42 (a)5 (v)16 (ery TJT]ding hup(dp=0TJT*(U)T01)s eMe

The Big Surprise: Part II

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not have sickle cell disease. She has sickle cell trait and will likely never have any problems. Most importantly is to let her know that she has sickle cell trait and if her future spouse does not have the trait, there is a 50% chance with each of her pregnancies, her children will also have sickle cell trait. Of even greater concern is that if she marries someone with the trait there is a 50% chance that with each pregnancy, the child will have sickle cell disease. The question that plagued Isabella the most was the most difficult to ask, "How long will I live?" Dr. Hernandez explained

that sickle-beta-plus thalassemia tends to be the mildest form of sickle cell disease and that survival, as best we know, closely parallels that of the general population. This provided some relief to Isabella. Dr. Hernandez thought for one visit, they were off to a good start regarding the young couple's understanding of what sickle cell trait and disease entails. He further assured them he would be there for them and to approach their bright futures with an open mind. He went on to tell Isabella there are some routine tests he likes to monitor annually in all of his sickle cell patients and

that if there is anything ever of concern he would notify her and bring her back in. Other than this, he would like to see her in follow up every six months for now. As the young couple left they felt somewhat better but still less certain about their futures, whether or not they would have more children, and would they stay in Castle Rock. For now they took peace in what they had, family, and decided they would do whatever was required to make sure their family was healthy and happy.

Fact: In Alabama mandatory newborn screening for sickle cell, independent of racial designation, was implemented in 1988. Since 1988, 5-8% of all babies born in Alabama, racial designated as white, test positive for sickle cell trait.

Your help is needed to learn more about the transition from pediatrics to adult care!!

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What is the purpose of this study is to learn more about the

