ORT_23 - The impact of the immunobiological Crizanlizumab in Sickle Cell Disease

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Introduction: Vaso-occlusion is a hallmark feature of sickle cell disease (SCD) that promotes ischemia-reperfusion injury and leads to acute pain episodes, known as vaso-occlusive crises (VOCs). VOCs are the primary reason for medical facility visits amongst SCD patients and are associated with increased morbidity and mortality. The development of new SCD therapies that have been shown to reduce or prevent VOCs like crizanlizumab—a humanized monoclonal antibody. The mechanism of action is the blockade of P-selectin, a protein present in the endothelium, which precipitates the release of pro-inflammatory substances with consequent vasoconstriction and consumption of nitric oxide.

Objective: To evaluate the impact of the use of crizanlimubab in the reduction of VOCs episodes in SCD.

Methodology: A literature review carried out and 12 complete articles from the period 2017 to 2021 were included. The descriptors used were: “Crizanlizumab AND Sickle Cell Disease AND VOC”, according to Medical Matters Headers, in the MEdLine/PubMed and SciELO databases and 19 papers were excluded, as it was not possible to identify the full text or did not fulfill the scope of the search.

Results: A reduction in VOCs rates was evidenced with the use of the immunobiological crizanlizumab. The double-blind study SUSTAIN (2017) showed that regardless of the dose used (2.5 or 5mg/kg) the drug was efficient in reducing or attenuated the severity of VOC. The study also points out that 38% of patients on 5 mg/kg doses of crizanlizumab and 16% of patients on 2.5 mg/kg doses had no VOC during the study, supported by the 2019 SUSTAIN study arm and by the SUCCESSOR 2020 study, which had similar data regarding reductions and time interval between VOCs, suggesting a long-term effect of the drug. Confirming the long-term effect, the 2020 SUSTAIN study demonstrated that crizanlizumab treatment can reduce by up to 57% the annual number of days than other parenteral and oral opioid drugs that are used to administer VOC in SCD. Souza et al (2021) reported that the use of the drug can still present a significant difference in the reduction of the levels of extracellular vesicles derived from platelets, substances that are explored because they are biomarkers of clinical severity. The SPARTAN Trial suggests that the drug may reduce priapism episodes in SCD.

Conclusion: Several studies associated the number of VOC and risk of death in SCD, so the possibility of using a drug like crizanlizumab that reduces pain episodes, decreases the disease severity score and improves the survival of these patients is worthy of attention and further studies.

Keywords: Vaso-occlusive crises; Sickle cell disease; Crizanlizumabe