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ADHESION TO VCAM-1 AND P-SELECTIN PREDICT TIME-TO-RESOLVE (TTR) OF VASO-OCCLUSIVE CRISIS

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Background: Sickle cell disease (SCD) is characterized by frequent and unpredictable vaso-occlusive crises (VOCs) resulting in increased morbidity and mortality. There are no reliable biomarkers to predict the onset and progression of VOCs, complicating disease management. Cell-to-endothelium adhesion at P-selectin and VCAM-1 was shown to significantly contribute to VOC events.

Methods: Standardized, flow-based adhesion bioassays measuring whole blood adhesion to VCAM-1 and P-selectin were used in a 6-month longitudinal study with blood samples collection from SCD subjects every 3 weeks at baseline and during VOC with patient-reported VOC events and return to steady state captured by e-diary. Time-To-Resolution from VOC (TTR) was defined as that reported within one week of the preceding VOC.

Results: Flow Adhesion to P-Selectin during VOC and to VCAM-1 at baseline strongly correlated with TTR with about 50% predictive value; increased to 68% for a combination of these two markers. Inflammatory mediators (e.g. interleukins) and reticulocytes (%), combined with [these biomarkers further increased the multi-parametric model predictive value up to 75-80%. Notably, adhesion on P-Selectin at baseline and on VCAM-1 at VOC lacked significance for predicting TTR.

Conclusions: Times-to Resolution of VOC were found to be highly patient-specific and linked to patient ' blood biochemical and hemodynamic properties. Within study limitations related to the sample size and VOC-related interventions, the data indicate that VOC resolution time can be predicted with the use of flow adhesion and biochemical markers. If validated, such combinations can be utilized for adapting and selecting treatments best suitable for individual patients.