Deployment of Red Cell Health Biomarkers at Sickle Cell Disease Pilot Sites

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BACKGROUND

- Diagnostic technologies to assess red blood cell (RBC) health in sickle cell disease (SCD) are inadequate.
  - Poorly validated, outdated, and lack global standards
  - Not routinely used in clinical decision making for SCD
- There is a critical need to validate SCD biomarkers to improve care for these patients.
  - Monitor response to therapy
  - Predict impending vaso-occlusive episodes (VOEs)
  - Stratify patients based on disease severity
- Recent surge in the development of SCD-modifying therapies target novel mechanisms of action to improve RBC health
  - Increase of hemoglobin oxygen affinity
  - Direct inhibition of p-selectin adhesion
  - Reduction of RBC oxidative stress
  - Induction of fetal hemoglobin
- We **hypothesize** that broad access to validated biomarkers of RBC health will enable more preventative models for SCD care by making RBC health a measurable target in the clinical setting.

OBJECTIVE

The objective of this study was to provide a qualitative, narrative description in deploying a specialized central lab model that focuses on RBC health biomarkers.

METHODS

Clinical Send-out Whole Blood (WB) Samples

- Drawn in sodium citrate vacutainers
- Shipped overnight at 2-8oC within 72hrs
- Ignite Medical Technologies
- Laboratory management system
- Critical results reported by phone call or HIPAA compliant text message alert

Pilot Clinical Sites

- Jan 2020 – Feb 2022
- Foundation for Sickle Cell Disease Research
- Children's Hospital of Michigan
- Detroit Medical Center Adult Sickle Cell Clinic
- Karmanos Cancer Center
- Children's National Medical Center

METHODS

Clinical send-out tests offered

- Flow adhesion of whole blood to VCAM
- Flow adhesion of whole blood to p-selectin
- Mechanical fragility

Class	Test	Units
Whole Blood Adhesion Index	VCAM1	cell/mm²
	PSEL	cell/mm²
Mechanical Fragility	MFI-3	3 min
	MFI-10	10 min
	PreExisting Hemolysis	Percent

Table 1 (above). Red Blood Cell Health (RBC) Biomarkers: Flow adhesion of whole blood to VCAM (0121U); Flow adhesion of whole blood to p-selectin (0122U); Mechanical fragility (0123U)

	Reference Range	
	Normal Population	**Steady State**
A.	<50	200-400
B.	<40	<50
C.	0.60-1.00	1.01-1.35
D.	5.00-5.75	6.25-7.25
E.	<0.04%	0.3%-1.8%

Table 2 (left). Reference range for RBC Health Biomarkers: A. Flow adhesion of whole blood to VCAM; B. Flow adhesion of whole blood to p-selectin; C. Mechanical fragility (MF3) ; D. Mechanical fragility (MF10); E. Per-existing hemolysis

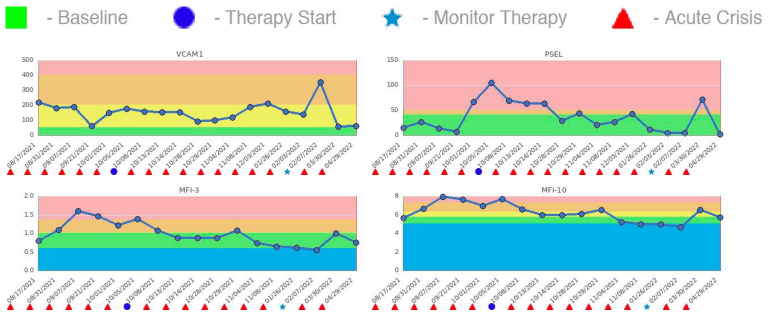

Figure 1. Indications for Testing: Longitudinal assessment of RBC Health Biomarkers over a 2-yr period in a SCD patient provides clinicians a tool to assess red cell health during acute crisis, baseline, and at the start of therapy and while on therapy.

Functional Fluidics ownership interest

SUMMARY OF RESULTS

- Sample Information: 11,550 individual tests on 3,850 individual clinical blood samples from 759 unique individuals with SCD
- Average turn-around time(TAT) for reporting results to the clinical site was 2.38 days from the date of sample accessioning
- Critical values reported: 740 or 3,850 samples
- Indications for testing included:
  - Acute crisis (n=2,291)
  - Baseline assessment (809)
  - Monitoring therapy (770)
  - Therapy start (69)
  - Unspecified (247)
- Individuals on SCD-modifying therapy:
  - Hydroxyurea (n=295)
  - Adakveo (n=54)
  - Voxelotor (n=55)
  - Endari (n=43).
  - 127 occurrences of combination therapy being used
  - 82 occurrences did not include hydroxyurea

Age Range (yrs)	N	Indication for Testing	N	SCD-Modifying Therapy	N	Turn-around time (TAT)
0-9	233	Acute Crisis	2291	Hydroxyurea (HU)	295	2.3 days
10-19	266	Baseline Assessment	809	Adakveo (Crizanlizumab)	54	Combination Therapy
20-29	122	Monitoring Therapy	770	Oxbryta (Voxelotor)	55	127
30-39	66	Therapy Started	69	Endari (L-glutamine)	43	Therapy Excluding Hydroxyurea (HU)
40-49	52	Other	247			45
50-59	20					

Table 3. Analysis of clinical send-out tests obtained over 2years from 5 pilot clinic sites:

SUMMARY

- Providers confirmed RBC biomarker data are helpful to:
  - gain more insight into individual patient cellular phenotype
  - assess response to therapy
  - encourage better compliance with chronic SCD-modifying therapies
- We established a feasible, specialized central lab model to increase clinical access to RBC health biomarkers.
- Multiple investigator-led collaborations are underway to leverage access to RBC health biomarkers to gain better post-market insight into the response to approved SCD-modifying therapies in the "real world".