Mapping Incidence of Post-Transfusion Malaria in an Endemic Population

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Background

The Johns Hopkins University-Makerere University Care Limited Research Collaboration oversees The Mirasol Evaluation of Reduction in Infections Trial (MERIT) Study in Kampala, Uganda. This double-blinded randomized control trial aims to test the safety and efficacy of the Mirasol pathogen reduction therapy on whole blood *in vivo.* "The objective of the MERIT study is to investigate whether Mirasol pathogen reduction therapy of whole blood can prevent seven targeted TTIs (malaria, bacteria, human immunodeficiency virus, hepatitis B virus, hepatitis C virus, hepatitis E virus, and human herpesvirus 8.)[1]" The study's primary funding source is the United States Department of Defense. The population participating in the project are Ugandan locals receiving care at the Mulago National Referral Hospital in Kampala, Uganda, who have agreed to participate in the MERIT Study.

Learning Objectives

1. Create a database for MERIT Study data.
2. Apply global health competencies and bioethics frameworks to analyze findings within the context of transfusion-transmitted infections.
3. Understand the differences in blood transfusion protocols globally.

Activities

- Data Analysis
- Data Consolidation
- Database Creation

Deliverables

- Data spreadsheet
  - Example charts and graphs based on analysis of existing data
- Website mock-up

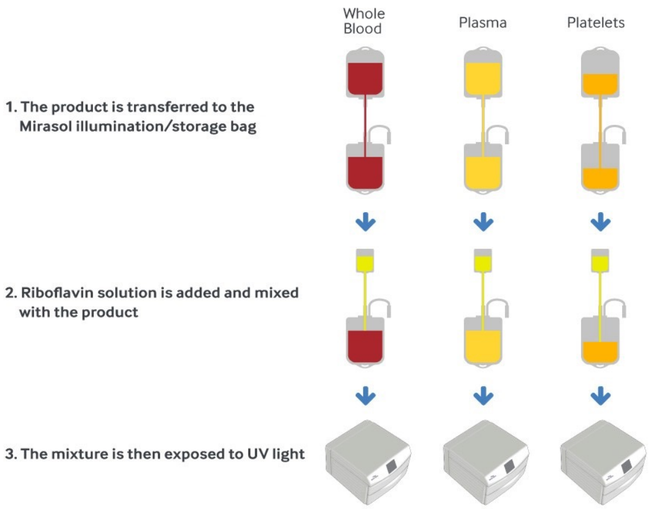

Figure 1—The Mirasol Process: *A breakdown of the Mirasol System for pathogen reduction in whole blood, plasma, or platelets.[2]*

Methods

Recruitment started in November 2019 and is expected to run until 2024. Two thousand patients will be enrolled and randomized (1:1) to receive either Mirasol-treated or standard-issue WB transfusions and followed up for ten weeks.[1]

We began receiving samples from Kampala, Uganda, in April 2022. We immediately began running polymerase chain reaction (PCR) assays to measure the species parasitic load of the blood samples collected from study participants. The PCR results were grouped as follows:

- Negative (<500)
- Low Positive (501-1000)
- High Positive (>1000)
- Questionable (Based on a line-by-line analysis)

These data were then used to determine the presence of malaria infection, also disaggregated by species. Finally, the prevalence of malaria infection and frequency per species were calculated for the 1,536 available samples. Next steps include the following:

- Continuing to analyze samples as they are processed
- Generating a database to work with the data more easily
- Assessing the safety and efficacy of Mirasol pathogen reduction therapy within the context of the MERIT Study

Of note, some repetition was required for some samples due to mechanical issues with the PCR machine. Additionally, the data represented here are not complete, as the study is ongoing.

		Study period (enrollment, intervention and post-intervention)						
		Enrolment	Intervention					
Time point				2-6 hrs	48 hrs	Day 7	Week 4	Week 10
Screening	Informed consent process	x						
	Eligibility assessment	x						
Enrolment	Demographic data	x						
	Pre-transfusion testing	x						
Intervention	Mirasol treated blood		x					
	Standard blood		x					
Assessment Efficacy Endpoint	Predefined viral, bacterial, or parasitic TTI				x	x	x	x
Assessment Safety Endpoint	Assessment for Transfusion reactions			x		x		
	Change in hemoglobin			x				
	Delayed transfusion reactions/neoantigenicity							x
	Adverse events			x	x	x	x	x

Figure 2—MERIT Study Schedule: *Broken down by enrollment, intervention, and assessments.[1]*

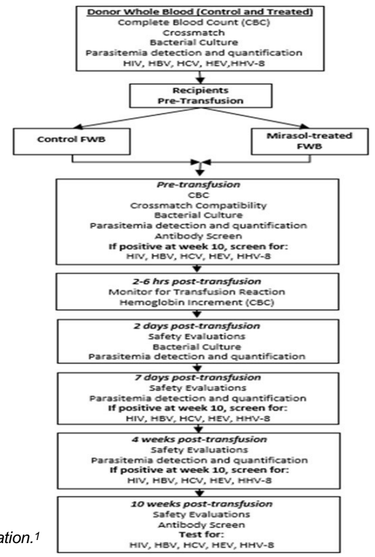

Figure 3—MERIT Study Evaluation Framework: *Donor blood and recipient evaluation.[1]*

Lessons Learned

A key takeaway from this experience was a greater appreciation for collaborative research efforts among universities, hospitals, and countries. It became clear that the best and most equitable type of research recognizes that this approach is essential to ensure positive outcomes. It also became evident that while this group effort may bring about positive change, stakeholders must also consider many systemic failures, such as differences in blood transfusion safety protocol. Keeping similar concepts in mind allows for a push towards building expectations around practical reality, thereby emphasizing a more localized approach to global health and public health practice.

Results

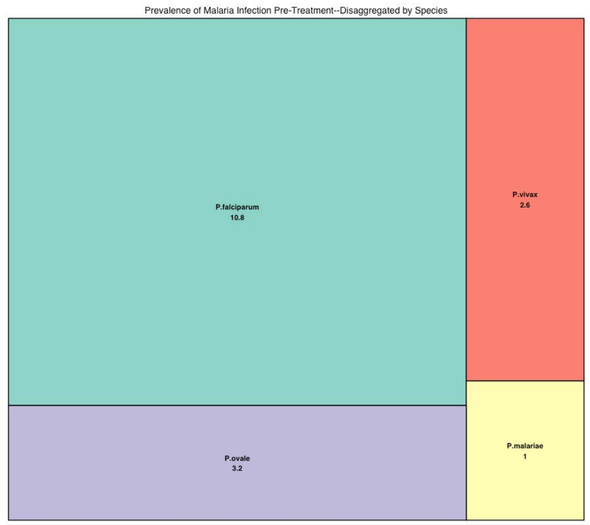

Figure 4—Pre-Treatment Malaria Prevalence: *Broken down by species. (n=)* $\frac{170}{959}$

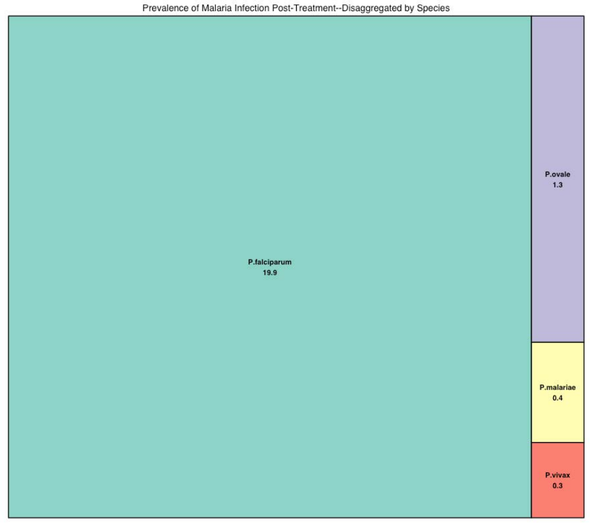

Figure 5—Post-Treatment Malaria Prevalence: *Broken down by species. (n=)* $\frac{154}{705}$

Public Health Implications

The most significant implication of this work on public health is its potential to redefine the process of blood transfusion worldwide. It was made clear throughout this process that the current approaches are neither equitable nor justice-based. Analyzing this data will allow for assessing data from the MERIT study while also providing a resource from which further studies could be developed.

References

1. Kasirye R, Hume HA, Bloch EM, et al. The Mirasol Evaluation of Reduction in Infections Trial (MERIT): study protocol for a randomized controlled clinical trial. Trials. 2022;23(1):257. doi:10.1186/s13063-022-06137-8.
2. Mirasol® Pathogen Reduction Technology. Accessed October 17, 2022. https://www.terumobct.com/mirasol

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