

Ebola Convalescent Plasma: Considerations for future outbreaks

Based on EVD-001 and -002 Monrovia; Liberia Nov 2014-Jan 2015

**For IPFA's Workshop on Improving Access to Plasma and Plasma Products in
the Southern African Region Dec 2015**

Dr J. D. van Hasselt (jamesvh@global.co.za)

SA/CR/0002/15a

Liberia: November 2014-January 2015

Ebola convalescent plasma trial EVD-001 and EVD-002

(Brief- to support set up; training; donor recruitment and donor health and safety)

Disclaimer: At the time that this trial was performed the presenter had no relationship with GSK. In addition, there was no direct or indirect involvement by GSK in EVD-001 or EVD-002.

From mid 2014- WHO and others call for
therapeutic blood and plasma strategy

Ebola: a call for blood transfusion strategy in sub-Saharan Africa

Burnouf, Thierry et al.

The Lancet , Volume 384 , Issue 9951 , 1347 - 1348

Sept. 2015

Experience up to 2014

Treatment of Ebola hemorrhagic fever with blood transfusion from convalescent patients.

Mupapa K, Massamba M et al

[J Infect Dis.](#) 1999 Feb;179 Suppl 1:S18-23.

N=8 cases (Kikwit; DRC 1995 outbreak)

Research and experience with EC plasma...

- Dye, et al.(PNAS, 2012): high-dose immune globulin effective in NHP
- Treatment of expat cases in US with ECP
- WHO encourage interest in emergency use of plasma

Need for further research

Is Ebola Convalescent Plasma (ECP) safe and effective?

If so, can ECP be collected and readily available for patients in Ebola-affected countries?

EVD-001 objectives

- Correlate anti-EBOV IgG in ECP with viral load in treated subjects
- Compare survival of subjects treated with and without ECP
- Assess safety of treatment (with and without ECP)

EVD -002 design (support arm for -001)

- Recruit EVD survivors
 - EVD within last 2 years
 - At least 60 days since disease onset
 - At least 28 days since discharge
 - 2 negative EBOV tests by RT-PCR
- Qualification
 - Adult, at least 50 Kg, with low risk history for TTI's
 - Hemoglobin \geq 12.0 g/dL, negative pregnancy test
 - Negative for TTI's (HIV, HBV, HCV, syphilis, malaria)

Donor health- anticipated challenges

Ongoing convalescence

- Unrecognized target organ damage-metabolic status?
- Chronic debility-nutritional/parasitaemia/ID's
- Environmental factors

- Stigma and social isolation

Speculative- collectively little experience of Ebola survivors at the time

EVD-001 status (Clinical RM data)

- 6 Subjects enrolled
 - 4 Subjects O pos (received ECP)
 - 2 Subjects A pos (no ECP available, managed with IV standard of care)
- Clinical Observations
 - Renal failure
 - ECP well tolerated, no related AEs
- Progress
 - Enrollment stopped due to decline in cases

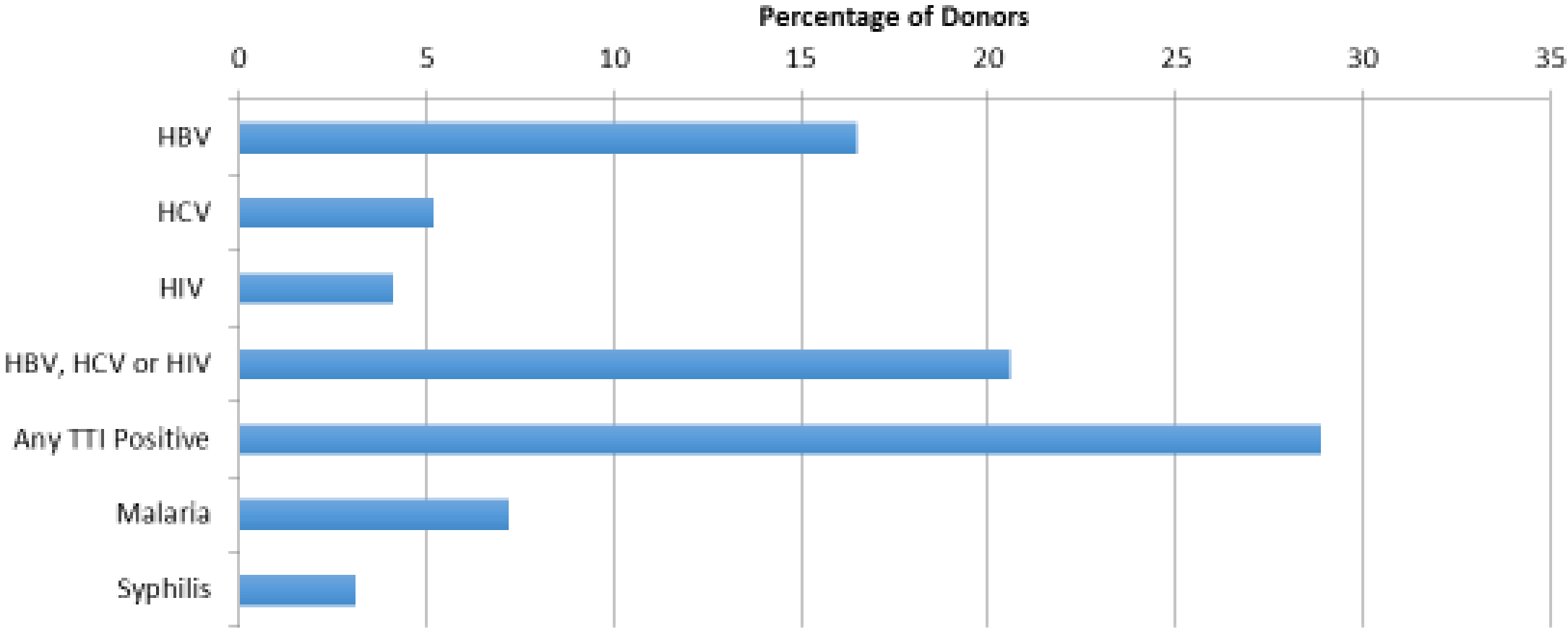
Other ECP Trials

- Guinea: Ebola-TX
 - Institute of Tropical Medicine, Antwerp
 - Donka Hospital, Conakry
 - Survival vs. historical controls
 - 103 subjects enrolled as of July 2015
- Sierra Leone: Ebola-CP
 - University of Liverpool
 - 34 Military Hospital, Freetown (*and Whole Blood trial*)
 - 4 subjects enrolled to date (3 treated with ECP)
 - +-50 ECP units collected

EVD-002 Donors (Clinical RM data)

- 97 participants
- 85 full-volume ECP units collected
 - **90.4% successful collection rate**
 - **39 units from repeat donors**
 - **<4% donated more than 2x**
- Age 33.8 ± 8.6 years (19 to 67)
- Weight 69.3 ± 11.4 Kg (50 to 112)
- Hemoglobin 13.83 ± 1.26 g/dL (11.6 to 17.1)

Transfusion Transmissible Infections (CRM data)



Outcomes wrt donor safety

- Observation - generally robust (Wt; Hb)
- Hypotensive episodes - nil reported
- Vasovagal-? one mild, late in procedure
- Citrate toxicity - nil
- Hydration status-overshoot

WELL TOLERATED AT THE TIME OF DONATION

Sequelae after Ebola virus disease: even when it's over it's not over

The Lancet Infectious Diseases, April 2015

Ebola Gone But Scars Remain: Survivors Deserve Better

FrontPageAfrica: Editorial August 31, 2015

Grim Snapshot Reveals Complex Health Issues for Ebola

Scientific American, September 2015

Condition of Scottish Nurse Suffering from Ebola Relapse

time.com ebola-nurse-critically-ill, Oct 15, 2015

Future considerations: Donor health

- Metabolic evaluation at outset and monitor
e.g. U&E/Creatinine/Ca/TP and Albumin*
- Inflammatory markers*
- Measure impact of plasma donation on convalescence
- Monitor and evaluate social impact-include sociologists/medical anthropologists in design and conduct

* PREVAIL study-NIH and Liberia MoH has enrolled 1500 survivors

Post Ebola acute relapse and chronic immune pathogenesis

Nurse admitted to Royal Free Hospital : relapse with Ebola meningitis

October 2015

Sanctuary sites...

Could regular, repeat plasma donation be a stressor?

Is ECP safe and effective?

Are Ebola survivors suitable for repeat plasma donation?

Is ECP a practical and appropriate therapeutic strategy?

(Assess alternative sources for Anti EBOV IgG e.g. Post immunisation?
Stable products such as Dried Plasma?)

Other considerations ?

Equipment

- Assume damage in transit-need back up
- Technical support unlikely
- Power supply unreliable/mismatch 110 spec vs 220 Volt mains
- Information management systems ?

In future

- Timely deployment-protocol and ethics ready to go
- Consider resource mismatch
- Prioritize ongoing clinical workload
- Continuity
- Logistics and technical support

Also consider

- Realistic technical spec -local infrastructure and capacity
- Anticipate legacy issues-skills, equipment, inventory.....
- Alert to unintended consequences –e.g. stigma, risk and vulnerability
- Align/support national programs

Zoonotic diseases and environmental change

Human Health

Animal Health

Environmental Health

= ONE HEALTH

What's next?

Conclusion

- Patient focused (equity)
- Extra vigilance re donor safety
- Local skills and legacy
- Research demands in context of clinical priorities
- Rigour -knowledge generation

Ethical Oversight Always

Transparency , Proportionality, Collaboration

Blood and Plasma community

- Emergency outbreak response team
- Database of willing and able personnel
- Commitment to provide resources-collective collaboration
- Realistic blueprint

Contribution to wider response

Collaboration with WHO Blueprint project for whatever comes next

THANK YOU

Acknowledgements:

- Liberian staff at ELWA and plasma donors
- Clinical RM kindly shared data (www.clinicalrm.com)
- B&MGF funded study plus support from WFP and others

James van Hasselt

jamesvh@global.co.za