Current Status of Filovirus Therapeutics
Overview

- SMALL MOLECULES
- SiRNA
- THERAPEUTIC VACCINES
- COMBINATION THERAPIES
Favipirivir

- **Bixler et al.; 2018, Antiviral Research 151:97-104**
  - Oral dosing not effective against EBOV or MARV-Musoke
  - 250/150 mg/KG BID IV dosing 0-13 dpi: 5/6 cynomolgus macaques survived MARV-Musoke challenge

Guedj et al.; 2018, PLOS Med 15(3) e1002535

- **JIKI TRIAL**
  - Favipirivir showed a good tolerance profile in patients with EVD but did not demonstrate a strong antiviral efficacy—presumably due to suboptimal dosing regimen that resulted in plasma drug concentrations below the EC50
BCX4430

- 3.4-16 mg/KG BID IM 48 hrs post challenge with EBOV in Cynomolgus macaques=delayed time to death, no survival.

- 25mg/KG BID IM 30-60 minutes challenge with EBOV in Rhesus= 6/6 survived.
  - Taylor R,. *J Infect Public Health*. 2016;9(3)

- 15mg/KG BID IM **24 and 48 hrs** post-challenge with MARV-Musoke treatment for 14 days, 6/6 cynomolgus macaques survive

- RAPIDE-BCV trial (single arm phase 2) Study stopped by manufacturer, no serious adverse reactions identified; only 4 participants enrolled-not possible to determine efficacy
SiRNAs

**AVI7537-Anti-sense Oligomer (VP24)** *(Warren TK, et al. 2015 mBio.;6(1))*

- 1 h ± 30 min after viral challenge once daily for 14 consecutive days 6/8 survived **EBOV-Kikwit** challenge

**AVI7288-Anti-sense Oligomer (NP)** *(Warren et.al 2016 PLOS NTD 10:2)*

- PMO treated 15mg/Kg once daily for 14 days with **latest dpi 4 days** resulting in 5/6 surviving cynomolgus macaques (83%) infected with **MARV-Musoke**

**siEbola-3 LNP (VP35)** *Thi, E. P. et al. 2015 Nature 521, 362–365*

0.5 mg/kg by bolus intravenous infusion 72 h after **EBOV-Makona** challenge then on days 4, 5, 6, 7, 8 and 9 (3/3 survived).

**RAPIDE-TKM trial:** After 14 adults had received TKM-130803, the pre-specified futility boundary was reached, and enrollment was stopped. *Dunning J, et al. (2016) PLOS Medicine 13(4)*

**siRNA-LNP (NP)** *(Thi et. al., 2017, JClinInvest, 127, 12)*

- siRNA-LNP treated for 7 days starting **4 days** PI protects 100% rhesus macaques **MARV-Ravn**
- NP siRNA-LNP treated for 7 days starting **4 days** PI protects 4/4 (100%) or **5 days** resulted in 2/4(50%) protected rhesus macaques against **MARV-Angola** challenge
**Remdesivir**

PREVAIL IV: A Randomized, Double-Blind, 2-Phase, Phase 2 Trial of Remdesivir vs Placebo for Reduction of Ebola Virus RNA in the Semen of Male Survivors  


*Porter et. al., 2020, JID, 222:1894-901
Combination therapy protects macaques against advanced Marburg virus disease

- Single 100 mg/Kg IV dose of MR-186-YTE starting 5 days PI with MARV-Angola
  - 5/5 (100 % survival)

- 10 mg/Kg loading/5 mg/Kg maintenance IV starting 5 days PI with MARV-Angola
  - 3/4 (75% survival)
Combinational Therapy Extends the Therapeutic Window in MARV-Angola infected NHP to 6 DPI

p = 0.0012
Postexposure Treatment of Marburg Virus Infection

Thomas W. Geisbert, Lisa E. Hensley, Joan B. Geisbert, Anders Leung, Joshua C. Johnson, Allen Grolla, and Heinz Feldmann

Immune correlates of postexposure vaccine protection against Marburg virus


Postexposure immunization can prevent disease and reduce transmission following pathogen exposure.
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