Overview of therapeutics R&D approaches for Bundibugyo Virus disease

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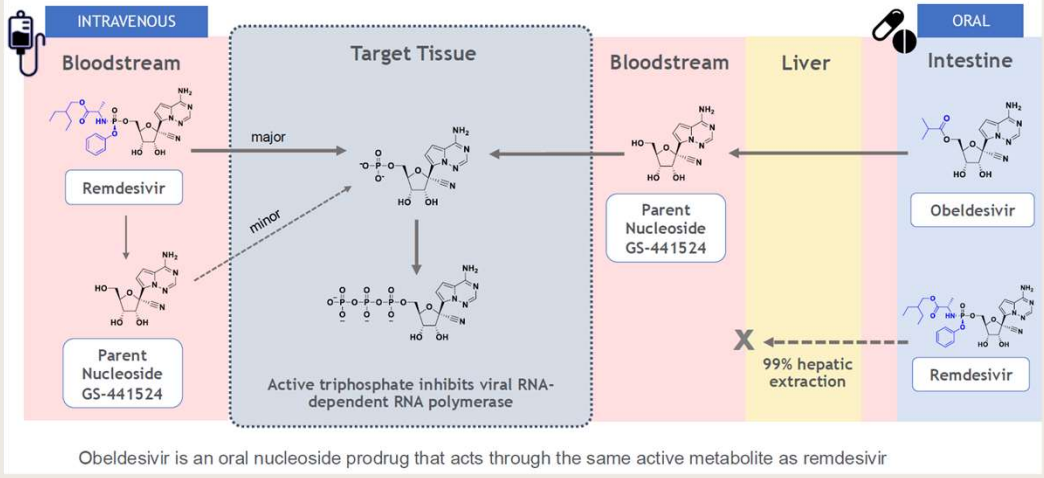
Remdesivir (RDV) and Obeldesivir (ODV) are prodrugs of the broad spectrum GS-441524 nucleoside analogue



Obeldesivir is an oral nucleoside prodrug that acts through the same active metabolite as remdesivir

In vitro activity for Bundibugyo virus similar to other filoviruses

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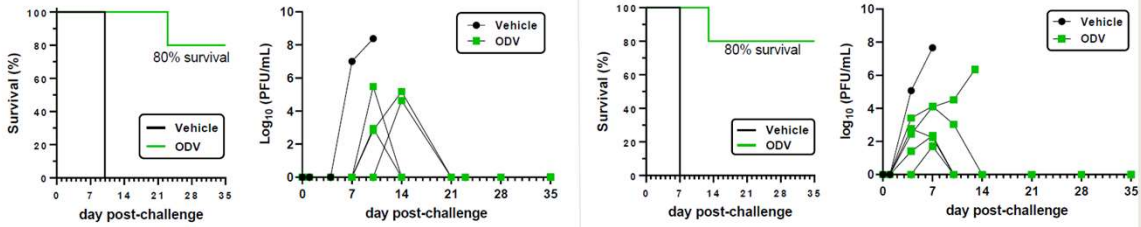
Obeldesivir for Post-exposure prophylaxis

3

Zaire ebolavirus and Marburg virus challenge in cynomolgus macaques with survival and plasma viremia endpoints

Zaire Ebolavirus (cyno)	Marburg Virus (cyno)
ODV (100 mg/kg) QD x **10 days** @ 1 dpc	ODV (100 mg/kg) QD x **10 days** @ 1 dpc



Challenge: 10,000 pfu *Zaire ebolavirus* (Strain Makona) mucosal in cynomolgus macaques

Challenge: 1000 pfu *Marburgvirus* (Strain Angola) IM in cynomolgus macaques

Cross RW, et. al. *Sci Adv* (2025)

Cross RW, et. al. *Nat Med* (2025)

Obeldesivir (ODV): 100 mg/kg PO QD x 10 days @ 1 day post-challenge (dpc); predicted to be equivalent to 350 mg BID human clinical dose based on plasma GS-441524 exposures

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MPB-134

Cocktail of 2 pan-Ebola virus monoclonal antibodies
Phase I data available

[A Two-Antibody Pan-Ebolavirus Cocktail Confers Broad Therapeutic Protection in Ferrets and Nonhuman Primates - ScienceDirect]

4

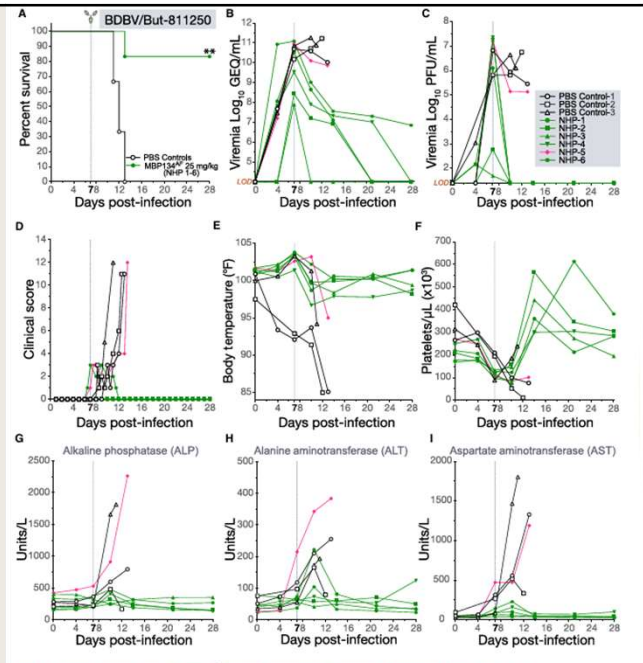

Figure 6. A Single 25-mg/kg Dose of MBP134^{AF} Protects Cynomolgus Macaques Challenged with BDBV/But-811250

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Inmazeb and maftivimab (REGN3479)

5

- Inmazeb® is a cocktail of three fully human monoclonal antibodies:
  - maftivimab (REGN3479), odesivimab (REGN3471) and atoltivimab (REGN3470) co-formulated in a 1:1:1 ratio
- Inmazeb® was tested in a randomized controlled clinical trial (PALM Study) during the 2018 Ebola Zaire outbreak in the Democratic Republic of Congo (N Engl J Med381(24):2293-2303)
  - 155 patients with confirmed Ebola infection (positive on RT-PCR) were treated Inmazeb®
  - Inmazeb® was statistically superior to ZMapp at 28-day mortality
  - Demonstrated to be have an acceptable safety profile (most common presenting symptoms were GI, fever, and headache)

- REGN3479 (mafitivimab) is the most potent neutralizing component of Inmazeb® and has broad activity *in vitro* against EBOV, SUDV and BDBV
- Importantly, both Inmazeb® and REGN3479 monotherapy demonstrated similar efficacy in guinea pig model of EBOV

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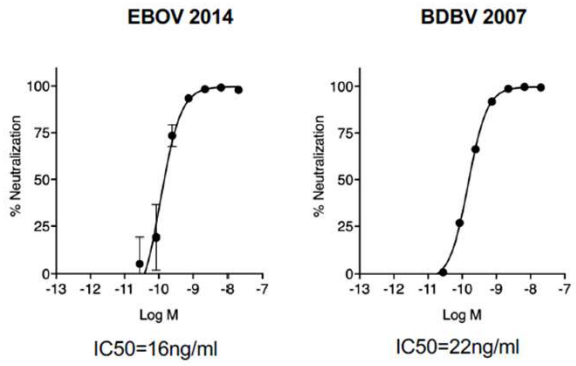
REGN3479 has similar neutralization potency against EBOV and BDBV

6



- The epitope of REGN3479 has been previously mapped using structural studies (Cell Host Microbe 2023 Feb 8;31(2):260-272.e7)

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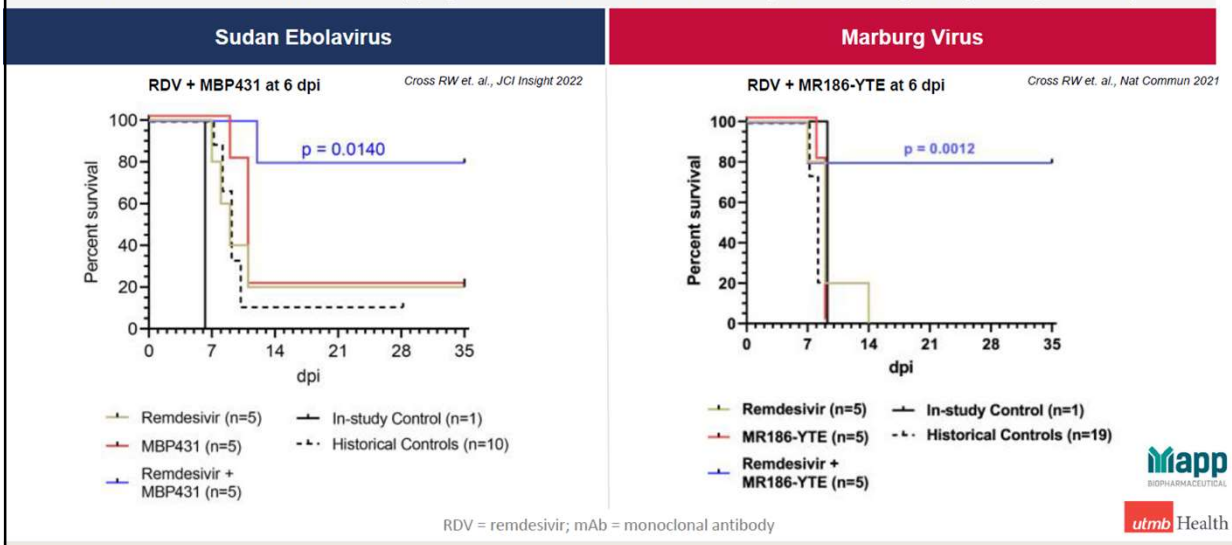
Combination therapy mAbs and remdesivir

7

Remdesivir + mAb Combination Therapy against Sudan Ebolavirus & Marburgvirus Challenge in Cynomolgus Macaques



RDV = remdesivir; mAb = monoclonal antibody

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Therapeutic Prioritisation TAG review

8

Monoclonal antibodies MPB-134 and maftivimab are to be prioritised for clinical investigations for treatment of BDBV disease

Remdesivir is also prioritized for treatment of BDBV disease including the option of combination therapy with monoclonal antibodies

The oral antiviral obeldesivir is prioritized for post-exposure prophylaxis with 10 days treatment duration

Monoclonal antibodies could be considered as well for post-exposure prophylaxis considering supply availability and feasibility of IV administration

Other small molecule antivirals and monoclonal antibodies will be revised in due course

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8


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Classified as internal/staff & contractors by the European Medicines Agency

9