Current status of filovirus immunotherapeutics

Larry Zeitlin, Ph.D.
larry.zeitlin@mappbio.com
OVERVIEW

- Ebola virus
- Sudan virus
- Pan-ebolavirus
- Marburg virus
Ebola Virus (Zaire ebolavirus): PALM trial

vs. ZMapp
Mab114: P=0.007
REGN-EB3: P=0.002

Ebola Virus (*Zaire ebolavirus*)

- **REGN-EB3 (Inmazeb®) from Regeneron**
  - 3 monoclonal cocktail, 150 mg/kg IV infusion
  - Approved by FDA in October 2020

- **mAb114 (Ebanga) from Ridgeback**
  - Single mAb, 50 mg/kg IV infusion
  - Approved by FDA in December 2020
Sudan Virus (*Sudan ebolavirus*)

- **MBP134 from Mapp Bio:** Phase 1 clinical study in progress
- **CM-JLD from Celdara Medical:** IND anticipated in Q1 2025
- **Monoclonals with non-human primate (NHP) proof of concept data**
  - IBT-T02 (Javad Aman, Integrated Biotherapeutics)
  - rEBOV-515 + rEBOV-442 (James Crowe, Vanderbilt University)
  - 1C3 + 1C11 (Erica Ollmann Saphire, La Jolla Institute for Immunology)
Sudan Virus: MBP134 (Mapp Bio)

- Cocktail of 2 human mAbs from an Adimab library with pan-\textit{Ebolavirus} activity
- Phase 1 dosing completed
- Lyophilized formulation in development
- Expanded access protocol in development
- Supported by BARDA, DTRA
Sudan Virus: MBP134 (continued)

Rhesus macaques (n=4/group)
Sudan Gulu (1000 PFU IM)
Treated Day 5
Sudan Virus: CM-JLD (Celdara Medical)

- Cocktail of 2 chimeric mAbs
- Supported by NIAID

Rhesus macaques (n=4/group)
Sudan Boniface (1000 PFU IM)
Treated with 50 mg/kg of cocktail D4 + D6

Herbert AS et al., Proc Natl Acad Sci USA. 2020 Feb 18;117(7):3768-3778
### Summary of SUDV NHP data

<table>
<thead>
<tr>
<th>Candidate</th>
<th>mAb dosing (days post inoculation)</th>
<th>Tested Dose</th>
<th>NHP</th>
<th>Challenge Strain</th>
<th>Treated Survival</th>
<th>Control Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>MBP134</td>
<td>5</td>
<td>25 mg/kg</td>
<td>Rhesus</td>
<td>Gulu</td>
<td>4/4</td>
<td>0/5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7.5 mg/kg</td>
<td>Rhesus</td>
<td></td>
<td>4/4</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>25 mg/kg</td>
<td>Rhesus</td>
<td>Boniface</td>
<td>4/4</td>
<td>2/4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7.5 mg/kg</td>
<td>Rhesus</td>
<td></td>
<td>4/4</td>
<td></td>
</tr>
<tr>
<td>CM-JLD</td>
<td>4 + 6</td>
<td>50 mg/kg</td>
<td>Rhesus</td>
<td>Boniface</td>
<td>4/4</td>
<td>2/4</td>
</tr>
<tr>
<td>IBT-T02</td>
<td>4 + 6</td>
<td>20 mg/kg</td>
<td>Rhesus</td>
<td>Boniface</td>
<td>6/6</td>
<td>1/2</td>
</tr>
<tr>
<td>rEBOV-515 + rEBOV-442</td>
<td>4 + 7</td>
<td>30 mg/kg</td>
<td>Rhesus</td>
<td>Gulu</td>
<td>5/5</td>
<td>1/9</td>
</tr>
<tr>
<td>1C3 + 1C11</td>
<td>4 + 7</td>
<td>50 mg/kg</td>
<td>Cyno</td>
<td>Gulu</td>
<td>3/3</td>
<td>0/2</td>
</tr>
</tbody>
</table>

## Pan-ebolavirus mAbs

<table>
<thead>
<tr>
<th>Candidate</th>
<th>EBOV efficacy</th>
<th>SUDV efficacy</th>
<th>BDBV efficacy</th>
<th>Bombali In vitro neutralization</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ferret</td>
<td>NHP</td>
<td>ferret</td>
<td>NHP</td>
</tr>
<tr>
<td>MBP134</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>IBT-T02</td>
<td>nt</td>
<td>+</td>
<td>nt</td>
<td>+</td>
</tr>
<tr>
<td>rEBOV-515 + rEBOV-442</td>
<td>nt</td>
<td>+</td>
<td>nt</td>
<td>+</td>
</tr>
<tr>
<td>1C3 + 1C11</td>
<td>nt</td>
<td>+</td>
<td>nt</td>
<td>+</td>
</tr>
</tbody>
</table>

nt = not tested

Marburg Virus (*Marburg marburgvirus*)

- MBP091 from Mapp Bio: IND submitted
- IBT-T03 from Integrated Biotherapeutics: IND anticipated Q1 2024
Marburg Virus: MBP091 (Mapp Bio)

- Single human mAb from a human survivor against RBS on GP
- Single dose
- Phase 1 expected to start Q2 2022
- Expanded access protocol in development
- Supported by BARDA, DoD, NIAID

Mire CE et al. Sci Transl Med. 2017 Apr 5;9(384).
Marburg Virus: IBT-T03 (Integrated Biotherapeutics)

- Single neutralizing mAb from an immunized NHP against a non-RBS epitope
- Neutralizes Marburg and Ravn strains with sub-nM potency
- Phase 1 expected Q1 2024
- Supported by NIAID through Phase 1
Acknowledgements

- Dr. Brandy Houser, Celdara Medical
- Dr. Javad Aman, Integrated Biotherapeutics
- Dr. Ellen Monson, PI of MBP134
- Dr. Ronald Aimes, PI of MBP091