

EDİTÖRE MEKTUP / LETTER TO THE EDITOR

Ebola drug trial: a ray of hope

Ebola virüsüne yönelik ilaç çalışmaları: bir umut ışığı

Pugazhenthan Thangaraju¹, Shoban Babu Varthya², Sajitha Venkatesan³

¹Department of Pharmacology, All India Institute of Medical Sciences(AIIMS), Raipur, Chattisgarh, India ²Department of Pharmacology, Apollo Institute of Medical Science and Research, Andhra Pradesh, India ³Department of Clinical Division, Central Leprosy Teaching and Research Institute, Chengalpattu, India

Cukurova Medical Journal 2019;44(4):1532-1533.

To the Editor,

Ebola virus causes Ebola Viral Disease (EVD) associated with hemorrhagic fever in humans. The Ebola virus belongs to Filoviridae family¹. A new outbreak of dreadful virus named Ebola virus disease was declared in North Kivu Province by the Ministry of Heath on 1st of August, 2018 of Congo democratic republic. Earlier outbreak in west African countries caused heavy social and financial burden on those countries. In November 2018, WHO released a news on EVD stated as "New Hope with Ebola Drug Trial" bringing more hope to fight against deadly disease. Presently there are different drugs and vaccines are under trial to manage EVD. Among the these drugs like mAb114, Remdesivir, Zmapp and REGN-EB3 proved effective in controlling progression of disease in early stages of the trial. The present trial is planning to use mAb114 and Remdesivir combination is evaluated against Zmapp, the control arm. REGN-EB3 will be added to the trial in due course of time. mAb114 is a human monoclonal antibody currently in early stages of development. The mAb114 interacts with the Ebola virus glycoprotein (GP) trimmer and inner chalice of GP, remains associated following proteolytic removal of the glycan cap, and inhibits binding of cleaved GP to its receptor. This human monoclonal antibody has got potential towards EVD therapy and vaccine². Remdesivir (GS-5734) acts by RNA-dependent RNA polymerase (RdRp)-mediated mechanism and prevents its proliferation3, even in the setting of

(ExoN)-mediated exoribonuclease intact proofreading in viruses. In non-human primates, early initiation of polymerase inhibitors Favipiravir and Remdesivir improves survival, but whether they could be effective in patients is unknown⁴. Vincent Madelain et al.4 predicts survival rates of 60% for Favipiravir and 100% for Remdesivir when treatment is initiated within 3 and 4 days post infection, respectively. ZMapp is a combination of three humanized monoclonal antibodies, that was produced by the method of genetic modification of the most consumable tobacco plants, that target three Ebola virus major glycoprotein and its Epitopes. This monoclonal antibody drug has been shown survival benefit in experimental non-human primates that was infected with this Ebola virus⁵. A Randomized, Controlled Trial of ZMapp for Ebola Virus Infection appeared to be beneficial in EVD compared with standard care alone6. These molecules are the result of an earlier epidemic in west Africa. As the disease comes to control with active intervention, these trails are also not progressing. Keeping above views the WHO developed an ethical framework known as Monitored Emergency Use of Unregistered Interventions (MEURI E3/1.). Under this essential plan at the Ebola Treatment Centre in Beni in DRC now conducted trial under MEURI protocol. This is the first multi-drug trial for Ebola treatments and the major responsibilities lies in their rigorous collection of information and analysis of the authenticated data and this will deliver clarity about

Yazışma Adresi/Address for Correspondence: Dr. Pugazhenthan Thangaraju, Department of Pharmacology, All India Institute of Medical Sciences (AIIMS), Raipur, Chattisgarh, India Email:drpugal23@gmail.com Geliş tarihi/Received: 24.01.2019 Kabul tarihi/Accepted: 16.03.2019 Çevrimiçi yayın/Published online: 18.09.2019 which monoclonal antibodies works best for the dreadful viral condition in the current situation of wide outbreak with the team leading for the better care of Ebola patients. This trial will brings hope in management of ebolavirus. This will ultimately save lives in future outbreaks. These patients are provided optimal care along with administration of trial compound. It appears to be too early to conclude but the story of Kambale Kombi Vianey gives positive environment for future course of already tested compounds and resource targeting.

To conclude the first trial person acts as a messenger as well as the motivator to the risked patients. Being a person with all stigmatized and suffering, he an act as a media as well as the medium for dissemination of information to the public.

- Finansal Destek: Yazarlar finansal destek beyan etmemişlerdir. Author Contributions: Concept/Design : PT, SBV, SV; Data acquisition: PT, SBV, SV; Data analysis and interpretation: PT, SBV, SV; Drafting manuscript: PT, SBV, SV; Critical revision of manuscript: PT, SBV, SV; Final approval and accountability: PT, SBV, SV; Technical or material support: PT, SBV, SV; Supervision: PT, SBV, SV; Securing funding (if available): n/a. Peer-review: Externally peer-reviewed.
- Conflict of Interest: Authors declared no conflict of interest. Financial Disclosure: Authors declared no financial support

REFERENCES

- Jadav SS, Kumar A, Ahsan MJ, Jayaprakash V. Ebola virus: current and future perspectives: Infect Disord Drug Targets. 2015;15:20-31.
- Misasi J, Gilman MSA, Kanekiyo M, Gui M, Cagigi A, Mulangu S et al., Structural and molecular basis for Ebola virus neutralization by protective human antibodies: Science. 2016;351:1343–6.
- Agostini ML, Andres EL, Sims AC, Graham RL, Sheahan TP, Lu X et al. Coronavirus susceptibility to the antiviral remdesivir (GS-5734) is mediated by the viral polymerase and the proofreading exoribonuclease. mBio. 2018;9:e00221-18.
- Madelain V, Baize S, Jacquot F, Reynard S, Fizet A, Barron S et al. Ebola viral dynamics in nonhuman primates provides insights into virus immunopathogenesis and antiviral strategies. Nat Commun. 2018;9:4013.
- McCarthy M. US signs contract with ZMapp maker to accelerate development of the Ebola drug. BMJ. 2014;349:g5488.
- Davey RT Jr, Dodd L, Proschan MA, Neaton J, Neuhaus Nordwall J, Koopmeiners JS. A randomized, controlled trial of ZMapp for Ebola virus infection. The PREVAIL II Writing Group, for the Multi-National PREVAIL II Study Team. N Engl J Med. 2016;375:1448-56.

Yazar Katkıları: Çalışma konsepti/Tasarımı: PT, SBV, SV; Veri toplama: PT, SBV, SV; Veri analizi ve yorumlama: PT, SBV, SV; Yazı taslağı: PT, SBV, SV; İçeriğin eleştirel incelenmesi: PT, SBV, SV; Son onay ve sorumluluk: PT, SBV, SV; Teknik ve malzeme desteği: PT, SBV, SV; Süpervizyon: PT, SBV, SV; Fon sağlama (mevcut ise): yok. Hakem Deģerlendirmesi: Dış bağımsız. Çıkar Çatışması: Yazarlar çıkar çatışması beyan etmemişlerdir.