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Short Communication

Post-exposure prophylaxis following high-risk contact with Ebola virus, using immunotherapies with monoclonal antibodies, in the eastern Democratic Republic of the Congo: an emergency use program

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ABSTRACT

Introduction: With the development of therapeutics and vaccine against Ebola virus disease (EVD), the question of post-exposure prophylaxis for high-risk contact has emerged. Immunotherapies (monoclonal antibodies [mAbs]) recently validated for treating infected patients appear to be a good candidate for protecting contacts.
Design: During the tenth EVD outbreak in the Democratic Republic of the Congo, we have administrated mAbs (Mab114 or REGN-EB3) to high and intermediate-risk contacts of EVD patients.
Results: : Overall, 23 non-vaccinated contacts received mAbs after a median delay between contact and post-exposure prophylaxis of 1 day (interquartile range 1–2). All contacts were free of symptoms, and all had negative reverse transcriptase-polymerase chain reaction 14 days after the contact.
Conclusion: Immunotherapies appear to be promising candidates to protect EVD contacts. Interaction with vaccine needs to be analyzed and a larger study on efficacy conducted.

Introduction

Over the past decade, there have been significant advances in the management of Ebola virus disease (EVD), including the development of a vaccine (VSV-ZEBOV-GP, ERVEBO, Merck, USA) indicated for ring vaccination of contacts (Henao-Restrepo et al., 2017), and two immunotherapies (MAb114 and REGN-EB3) effective against mortality in patients infected with Ebola virus (EBOV) (Mulangu et al., 2019). Consequently, new strategic and operational issues have also emerged, including protection of high-risk contacts, defined as post-exposure prophylaxis (PEP).

Vaccination with ERVEBO is beneficial for breaking the transmission chains for EVD but has no place in PEP because antibody production occurs after 10 days (Fischer et al., 2018; Iversen et al., 2020). Monoclonal antibodies (mAbs) represent a good therapeutic option to be evaluated in PEP, as they effectively reduce mortality when administered early in the course of the disease and are easy to administer as they require only one intravenous injection.

Design

During the tenth EVD outbreak in the Democratic Republic of the Congo, national response teams and caregivers of the non-governmental organization The Alliance for International Medical Action administered MAb114 or REGN-E3B on an emergency-use basis for high-risk contact (direct contact with skin barrier breach with a confirmed EVD patient) and intermediate-risk contact (di-

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rect contact without skin barrier breach with an EVD patient), according to the WHO classification.

Results

Between 1 July 2019 and 31 January 2020, teams at the Ebola treatment centers in Beni, Katwa and Mambassa administered MAb114 (N = 21) or REGN-E3B (N = 2) to 23 individuals. These individuals had never received any Ebola vaccine. The median age of the participants was 30 years (interquartile range (IQR) 20–43) and 14 (61%) were female. Among them, 8 (35%) were children <10 years old, 2 of whom were treated at birth (in utero exposure from EBOV-infected mothers). Only 4 participants were health care workers. The contact was high-risk for 18 (78%) individuals and intermediate-risk for 5 (see table). The median time from contact to the administration of mAb was 1 day (IQR 1–2). The participants were monitored until day 14 by reverse transcriptase-polymerase chain reaction (RT-PCR) and on-demand clinical follow-up. No participants developed symptoms of EVD and all RT-PCR tests were negative.

Discussion

The secondary attack rate of EVD in the literature ranges from 37% for direct contact to 80% for handling dead bodies (Bower et al., 2016). The use of mAbs in PEP has been shown to be effective in mice and non-human primates (Brannan et al., 2019; Froude et al., 2018). In addition, 4 health care workers have previously been treated with a combination of mAbs and the antiviral favipiravir after intermediate or high-risk exposure; none of them developed EVD (Jacobs et al., 2015).

However, certain points need to be discussed. First, the World Health Organization's definition of contact cases does not mention the source patient's clinical status. It seems likely that contact with a patient with 'wet' Ebola (secretions, vomiting/diarrhea or external bleeding) is more likely to result in contamination than contact with a 'dry' Ebola case. In addition, the notion of skin barrier breach, which classifies contact as high-risk, is not always easy to identify in the field, particularly when it occurs despite personal protective equipment. Therefore, we propose that PEP be offered to individuals who have had direct contact (with or without skin barrier breach) with a confirmed case of 'wet' Ebola. Second, mAbs do not provide sustained immunity and vaccination is subsequently mandatory. However, ERVEBO and mAbs share the same viral target, the envelope glycoprotein (GP) (Cagigi et al., 2018). Therefore, it is likely that the vaccine will be inhibited by mAbs, especially when administered concomitantly (Fischer et al., 2018). Third, the overall protection strategy (PEP and vaccination) needs to be assessed in terms of feasibility. If the PEP alternative is more effective when administered soon after contact, as in our study, any strategy that leads to a delay, e.g., a few days after vaccination as proposed by Cross et al. (Cross et al., 2020), might decrease the efficacy and therefore render it an unsatisfactory operational option. On the other hand, both the minimum time between mAb and vaccine and the maximum time between contact and PEP administration remain to be defined.

Conclusion

In conclusion, the use of mAbs in PEP represents an attractive option in the protection of those who have had contact with an EVD patient; however, phase 2 and phase 3 studies to validate the effectiveness of this strategy are required, and the issues of feasibility and mAb-vaccine interaction need to be addressed.

Author contribution statement

Marie Jaspard (MJ), Sylvain Juchet (SJ), Beatrice Serra (BS), Denis Malvy (DM) designed the study. MJ, SJ, BS, Baweye Mayoum (BM), Issa Malam Kanta (IMK), Seto Camara (SC), Placide Mbala (PM) and Richard Kojan (RK) set up the study, enrolled and followed the patients and recorded clinical data.

MJ, SJ, DM had access to the raw data and performed the analysis.

MJ, SJ, DM drafted the manuscript.

All authors revised the manuscript critically for important intellectual content and approved the final version before submission.

Conflict of interest

All authors declare no conflict of interest

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Ethical considerations

The use of mAbs for Ebola virus disease patients was approved by the National Ethics Committee in the Democratic Republic of Congo within the PALM trial (University of Kinshasa). Each administration of mAbs in this pilot post-exposure prophylaxis emergency use was approved by the Ebola response committee led INRB (institute de recherche biomedicale), Kinshasa.

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