Study: Experimental Ebola drug ZMapp may benefit patients, but insufficient data

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According to initial results from a randomized, controlled trial of the experimental Ebola treatment ZMapp, the monoclonal antibody cocktail was well-tolerated and showed promise. Due to decreasing incidence in Ebola, the study could not enroll enough volunteers to determine definitively whether it is a better treatment for Ebola virus disease (EVD) than supportive care only. Initial findings from the clinical trial known as PREVAIL II were presented today at the Conference on Retroviruses and Opportunistic Infections in Boston.

ZMapp, developed by Mapp Biopharmaceutical Inc., based in San Diego, is composed of three different laboratory-made antibodies. The PREVAIL II study launched in March 2015 through a clinical research partnership between the Liberian Ministry of Health and the National Institute of Allergy and Infectious Diseases (NIAID), part of NIH. The study sought to determine if ZMapp plus the optimized standard of care for treating EVD—providing intravenous fluids, balancing electrolytes needed to maintain bodily functions, and maintaining healthy oxygen and blood pressure levels—was superior to the optimized standard of care alone in reducing deaths caused by Ebola virus disease. This collaboration then expanded to include research partners within the countries of Sierra Leone and Guinea as well as the French research organization INSERM.

The trial enrolled 72 adults and children with confirmed Ebola infection from Guinea (12 patients), Liberia (5 patients), Sierra Leone (54 patients) and the United States (1 patient). Investigators originally aimed

to enroll 200 participants, but closed enrollment at the end of January 2016 as the West Africa Ebola outbreak ended. All participants received the optimized standard of care, and half were randomly assigned to also receive three intravenous infusions of ZMapp administered three days apart.

Investigators compared the number of deaths in each group at 28 days after enrollment. Of the 71 patients included in the analysis (one patient left treatment), 21 died—an overall fatality rate of nearly 30 percent. Thirteen deaths were reported in the group of 35 patients who received only the optimized standard of care (39 percent), while eight deaths occurred in the ZMapp group of 36 patients (22 percent). The difference was not statistically significant.

Investigators noted that in both groups, having a higher virus level at study entry increased the risk of death. Fifty-three percent (16/30) of patients with high virus levels died versus 12 percent (5/41) of those with lower virus levels. Among those with high virus levels, 60 percent (9/15) receiving standard-of-care only died compared to 47 percent (7/15) of those who also received ZMapp. In the group with lower Ebola virus levels, 20 percent (4/20) receiving only standard-of-care died versus 5 percent (1/21) of those who also received ZMapp. In general, regardless of virus levels, those who received ZMapp appeared to do better, but the results were not statistically significant.

Investigators hope to follow the surviving participants for up to one year to assess any potential medical issues that might be related to EVD or use of ZMapp. In collaboration with NIAID, ASPR's BARDA continues to support the advanced development of Mapp's ZMapp monoclonal antibody therapeutic towards FDA approval.

More information: These findings were presented today at the 23rd Conference on Retroviruses and Opportunistic Infections at the John B.

Hynes Veterans Memorial Convention Center in Boston.

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