First trials of blood-based Ebola therapy kick off

Trials of 'convalescent' plasma have begun in Liberia, and plasma and blood studies in Guinea and Sierra Leone will follow.

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Michel du Cille/The Washington Post/Getty

Emmanuel Saah after leaving his handprint on a tribute wall for Ebola survivors at the ELWA 3 treatment centre in Monrovia.

The first clinical trials are starting in West Africa to test whether transfusing patients with plasma or blood donated by Ebola survivors is safe and effective in reducing illness and death.

The hope is that antibodies against Ebola that are present in survivors' blood might have a protective effect in those infected with the virus. Although some patients have been given such 'convalescent' blood or plasma alongside other care, it is unclear whether it is safe and effective because no proper clinical trials have yet been done.

The therapy would have the advantage that it could be scaled up quickly — there are now thousands of people who have survived Ebola in West Africa, many of whom are potential donors. By comparison, the Ebola vaccines that are currently under development might not be produced and deployed fast enough to help in the current epidemic, even if they prove to be effective. There is also no approved drug treatment for Ebola, which in this epidemic has a fatality rate of around 70%.

Convalescent blood therapy was discovered by the Prussian scientist Emil von Behring as an effective treatment for diphtheria and tetanus, work for which he won the first ever Nobel Prize in Physiology or Medicine in 1901. The therapy was widely used in the first half of the twentieth century to treat many infectious diseases, ranging from hepatitis A to poliomyelitis. It fell out of use with the development of antibiotic and antiviral drug treatments, although it is still used to treat some diseases, including Argentine haemorrhagic fever, a rodent-borne illness that is endemic in parts of Argentina. Antibodies extracted specifically from plasma — the fluid in which blood cells are suspended — are also used to treat several diseases, such as rabies and botulism.

Liberia trial

The first trial of the convalescent therapy began in Liberia late last week with the collection of plasma from survivors at the ELWA 2 hospital in Monrovia and the transfusion of the trial's first patient.

The trial is being funded by the Seattle-based Bill & Melinda Gates Foundation as part of its US$5.7-million support for developing and testing experimental Ebola treatments. It is being organized by ClinicalRM, a contract research organization in Hinckley, Ohio, in coordination with national health authorities and the World Health Organization (WHO).

The study will involve around 70 subjects, says David Hoover, a senior scientific adviser at ClinicalRM. That will include a comparison group of Ebola patients who will not receive plasma but will otherwise be given the same standard of care as the treatment group, Hoover says. The comparison group will contain patients who would not be eligible for treatment because their blood type is incompatible with that of any of the available plasma.

The trial's main goal is to test whether antibodies lower viral load. The small size of the study and the difficulty of working in the midst of an epidemic mean that it may not be possible to conclusively establish whether the therapy can save lives. It will take about ten weeks to enroll all the patients in the study, and results will be shared as soon as possible, Hoover says.

Guinea trial

At the end of the year, a large consortium of European and African research and blood-transfusion organizations will start a separate trial in Guinea. The study, which has €2.9 million (US$3.6 million) in funding from the European Union and further support from the London-based biomedical charity the Wellcome Trust, will be done in cooperation with the humanitarian organization Médecins Sans Frontières (also known as Doctors Without Borders) at its Donka Ebola treatment centre in Conakry.

The Guinea trial will involve 200 to 300 patients, with a comparison group as in the Liberia trial. With its larger size, it will aim to assess the effect of the therapy on survival rates 14 days after treatment.

Johan van Griensven, a clinical researcher at the Institute of Tropical Medicine in Antwerp, Belgium, who is coordinating the Guinea trial, says that the plan is to begin evaluating convalescent plasma in late December or early January.

Blood versus plasma

Using whole blood is less complicated than using plasma, which must first be separated from blood by centrifugation. For responses to an epidemic, however, plasma is preferable, because the remaining red blood cells can then be pumped back into the donors' bodies. This means that survivors can donate up to a litre of plasma, depending on their body weight, every two weeks, whereas whole blood can be donated only once every three to four months. Plasma can also be preserved for a year, whereas whole blood lasts for only a month or so.

The results of the Guinea trial could be available within two months or less, says van Griensven, adding that he is "moderately optimistic" that the therapy will be effective.

In preparation for the trials, the organizers, together with national authorities, the WHO and other international agencies, have been working to reinforce the region's blood-transfusion infrastructure — which in many places was almost non-existent. They have been training health-care workers and providing tools to screen donated blood for pathogens such as HIV.

Convalescent blood and plasma would seem to be plausible treatments for Ebola, given that tests of an experimental cocktail of monoclonal antibodies known as ZMapp gave 100% protection against the virus in rhesus macaques, says Calum Semple, a paediatrician and clinical virologist at the University of Liverpool, UK, who is involved in the trial in Guinea.

But, he adds, only clinical trials can establish whether the therapy works. If it does, production of convalescent serum will be scaled up immediately in West Africa.

In Sierra Leone, the third of the three countries most affected by the epidemic, the group Sierra Leone Action plans to launch its own trials of convalescent plasma. Created by researchers and clinicians in the country and by Sierra Leoneans who have emigrated, the group hopes to begin collecting plasma later this month.

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Updates

Updated:A previous version of this article stated that the Guinea trial was to start evaluating blood-transfusion therapy before moving

on to plasma. The article has been updated as *Nature* has learned that the whole-blood phase has been dropped.