CLINICAL TRIALS FOR ZIKA VIRUS INFECTION

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Introduction

Zika virus (ZIKV) is transmitted to humans throughout bites of *Aedes aegypti* (Linnaeus) and *Aedes albopictus* (Skuse) mosquitoes. ZIKV infection may be asymptomatic in most cases, but it may cause fever, headache, muscle pain, rash, and may be associated with Guillain-Barré syndrome (1). Furthermore, the Pan-American Health Organization informed a total of 3,715 cases confirmed of the congenital syndrome associated with ZIKV (CSZ) infection in the Americas from 2015 – 2017 (2), which may include microcephaly, eye abnormalities, craniofacial disproportion, or articular deformities (3). Currently, there are no vaccines or drugs approved for the treatment of ZIKV infection (1,3). Clinical trials are research experiments done in humans after being done in animals after designed to answer specific questions about interventions (e.g. vaccines, drugs, dietary supplements, or medical devices) for further study and comparison. These trials generate important information on safety and efficacy and are only conducted after a national health authority committee approval (4). They are conducted in four phases: *Phase I* – new biomedical intervention in a small group of people (e. g., 20- 80) for the first time to evaluate the safety, safe dosage range, and to identify side effects); *Phase II* – biomedical or behavioral intervention in a larger group of people (several hundred) to determine efficacy and to further evaluate its safety. *Phase III* – biomedical or behavioral intervention in large groups of human subjects (from several hundred to several thousand) by comparing the intervention to other standard or experimental interventions as well as to monitor adverse effects, and to collect information that will allow the intervention to be used safely; *Phase IV* – conducted after the intervention has been marketed. These studies are designed to monitor the effectiveness of the approved intervention in the general population and to collect information about any adverse effects associated with widespread use (4).

Method

To verify the existence of clinical trials of ZIKV infection treatments, a search was performed on July 21, 2020, at the clinicaltrials.gov database, with the descriptor [zika] at the simple search field.

Results / Discussion

In our search, we did not find any new drug or another FDA-approved drug in repurposing clinical trials for ZIKV treatments. So far, 2 antibody products and 15 new vaccines are undergoing clinical trial evaluation as can be seen in **Table 1.** The NIAID vaccine involving DNA technology is the only one in clinical trials from phase II and all other products, vaccines or antibodies are in phase I. Furthermore, NIAID is the major Clinical trial sponsor for ZIKV vaccines with a portfolio involving several different technologies: live attenuated and inactivated vaccines, DNA and RNA vaccines, and a vaccine involving the saliva peptide for *Aedes* mosquito. This last technology, if approved, may help in the elimination not only of ZIKV but many flaviviruses transmitted by *Aedes* mosquitoes, like Dengue, Chikungunya, Mayaro fever, Yellow fever, West Nile Fever, St Louis, and Japanese encephalitis viruses.

As ZIKV outbreaks have ceased and are not easy to be predicted, the vaccine development is compromised due to the difficulty of testing in the absence of infected people (5). Nevertheless, although any Brazilian Company or public Institution sponsored any of these trials, on October 27, 2016, Sanofi Pasteur announced an agreement of collaboration with the Oswaldo Cruz Foundation and the Walter Reed Army Institute of Research (WRAIR) (6). Furthermore, on May 7, 2018, the Federal Hospital do Minas Gerais, Minas Gerais - Brazil, announced a clinical trial partnership with a DNA vaccine that was in phase II development (7). As can be seen in Table 1, the only vaccine with this portfolio under phase II is the DNA vaccine VRC-ZKADNA090.

Table 1 - Products undergoing clinical trial evaluation for ZIKV.

Clinical Trial	Product	Sponsor	Clinical Phase
NCT03624946	Polyclonal antibody (ZIKV-IG)	Emergent Biosolutions	I
NCT03443830	Monoclonal antibody (Tyzivumab)	Tychan Pte	I
NCT03425149	Total virus inactivated accine (VLA-1601)	Valneva	I
NCT02996461 NCT03110770	DNA vaccine (VRC-ZKADNA090)	NIAID	I II
NCT02840487	DNA Vaccine (VRC-ZKADNA085)	NIAID	I
NCT03008122 NCT02963909 NCT02952833 NCT02937233	Virus inactivated vaccine (ZPIV)	NIAID	I
NCT02996890	Viral prME recombinant vaccine (MV-Zika)	Themis Bioscience	I
NCT03611946	Live atenuated vaccine (rZIKV/D4Δ30-713)	NIAID	I
NCT03055000	A vaccine with peptides of mosquito saliva (AGS-v)	NIAID	I
NCT02809443 NCT02887482	DNA vaccine Vaccine (GLS-5700)	Geneone Life Science	I
NCT03343626	Total virus inactivated vaccine (PZIV ou TAK-426)	Takeda	I
NCT03014089	mRNA vaccine (mRNA-1325)	Modernatx	I
NCT04064905	mRNA vaccine (mRNA-1893)	Modernatx	I
NCT03158233	Patient observation for Clinical Trials with a DNA vaccine	Sanofi/Curevac	Pre-recruiting
NCT04015648	Vaccine ChAdOx1 Zika (ZIKA001)	University of Oxford	I
NCT04033068	Viral prME recombinant vaccine (MV-Zika-RSP)	Themis Bioscience	I
NTC04478656	Purified Inactvated adsorbed ZIKV vaccine (BBV121)	Bharat Biotech Technologiy LTD	I

Conclusion

15 vaccines products are under development for ZIKV infection prevention. In our search, we also found 2 antibody products under clinical tests in phase I and we did not find any new drug or another FDA-approved drug in repurposing clinical trials for ZIKV treatments. NIAID is the principal sponsor and no Brazilian enterprise is sponsoring any clinical trial, but two different agreements of development were done by FIOCRUZ and UFMG, respectively, with Sanofi Pasteur/WRAIR and NIAID.

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