WHO ADVISORY COMMITTEE ON VARIOLA VIRUS RESEARCH

REPORT OF THE TWENTY-SECOND MEETING, GENEVA, 4–5 NOVEMBER 2020

GLOBAL INFECTIOUS HAZARDS PREPAREDNESS

World Health Organization

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CONTENTS

EXECUTIVE SUMMARY

The World Health Organization (WHO) Advisory Committee on Variola Virus Research (ACVVR) held its twenty-second meeting on 4–5 November 2020 by video conference. The recommendations of the Committee are summarized in the report.

Variola virus repositories
The Committee received reports on the variola virus collections held by the authorized repositories at the Federal Budgetary Research Institution - State Research Center of Virology and Biotechnology VECTOR, Federal Service for Surveillance on Consumer Rights Protection and Human Well-being (FBRI SRC VB VECTOR, Rospotrebnadzor), Koltsovo, Novosibirsk Oblast, Russian Federation, and by the Centers for Disease Control and Prevention (CDC), Atlanta, Georgia, the United States of America.

Research update
The Committee received reports on progress of approved research using variola virus. Twenty-six additional variola virus isolates held in the CDC collection had been sequenced. COVID-19 had delayed research during the year under review. The Committee recommended approval of four new proposals presented, two each from CDC and VECTOR, and continuation of previously approved projects.

Antiviral agents
Studies with tecovirimat were ongoing to meet regulatory authority post-marketing requirements. A paediatric formulation and an intravenous formulation were also under development. It was planned to assess tecovirimat in conjunction with vaccination with the approved modified vaccinia Ankara vaccine (MVA) in human volunteers. The safety of brincidofovir had been evaluated in clinical trials, with mild and reversible side effects, and regulatory approval was expected shortly. Study of analogues of ST-357, a possible second-line drug, had begun. VECTOR anticipated that phase 2 and 3 trials of NIOCH-14 would begin in 2021. VECTOR also proposed to test 15 new chemical compounds against variola virus in vitro. Both VECTOR and CDC continued to explore individual, or mixtures of, monoclonal antibodies. CDC's humanized mouse model had displayed sensitivity to variola infection with a disease profile reminiscent of human infection.

Vaccines
Studies of the approved MVA vaccine continued in different contexts, including for the prevention of human monkeypox in the Democratic Republic of the Congo; the vaccine had shown an excellent safety profile and a strong memory response in health workers two years after initial vaccination. Canada had extended indications for the vaccine to include prevention of monkeypox and other orthopoxviruses for persons at risk, making the MVA vaccine the first vaccine approved for a wider range of orthopoxviruses. The neutralizing antibody response of LC16m8, a third-generation vaccine licensed in Japan for prevention of smallpox, continued to be assessed. VECTOR continued development of VACΔ6, a 4th generation attenuated vaccinia vaccine, and phase 2 and 3 clinical trials were authorized; licensure in the Russian Federation was anticipated for 2022.

Diagnostics

VECTOR continued to assess an immunochemical test kit for rapid, point-of-care detection of orthopoxviruses; the assay was specific and easy to use and suitable for a field setting. CDC was continuing to improve both nucleic acid-based and protein-based rapid diagnostic tests; detection of variola in a lateral flow protein-based assay had shown promising results. The Committee recommended that both laboratories work towards developing test technology that would not require the use of live virus to validate, and that the advances observed during the COVID-19 pandemic could serve as a basis from which to further develop diagnostic techniques for orthopoxviruses.

Paleogenomics

Continuing previous discussions on the issue of research on human remains, where variola virus DNA may be the subject of investigation or an incidental finding, the Committee reviewed options for guidance, and recommended finalizing a risk assessment framework for handling of such DNA. WHO recommendations on the distribution, handling, and synthesis of variola virus DNA would be updated accordingly.

Conclusion

The Committee expressed support for the continued work on potential antiviral agents against smallpox, voicing concern about the time that may be required to develop monoclonal antibodies, and recommended that work continue on the vaccines and diagnostics in development. Regarding diagnostics, including point-of-care tests, the COVID-19 pandemic had led to the rapid development of technologies that may be applicable for orthopoxviruses, and the Committee urged researchers to propose alternative methods that would not require the use of live variola virus. Proposals presented prior to the meeting were recommended for approval. Other recommendations offered by the Committee are summarized in this report.