THE STUDY OF REACTOGENICITY, SAFETY AND IMMUNOGENICITY OF RECOMBINANT VARIOLA-AND-HEPATITIS B BIVACCINE FOR ORAL ADMINISTRATION IN HUMANS

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All variola vaccines existing in the world and developed today abroad are intended mainly for parenteral administration (scarification and intracutaneous ones), which has a number of essential drawbacks: low productivity at mass vaccination of humans, the risk of accompanying infections with other viral agents (HIV, T-cell leucosis virus, hepatitis C virus, etc.) in the process of vaccination, release of variolovaccine virus into the environment (uncontrolled transmission to non-vaccinated individuals). In this connection, based on the recombinant vaccine virus (VV) strain previously produced at SRC VB “Vector”, we are developing a variola and hepatitis B bivaccine for oral administration, which will not have these disadvantages due to the development of the tablet form. Increasing the safety of such vaccine for the organism as compared to cutaneous variola vaccination is associated with switching off the thymidine kinase gene of VV due to the insertion of the DNA fragment of HB virus encoding the synthesis of preS2-S protein. Thus, this vaccine will provide immunity both to variola and HB in the population.

In cooperation with the VC of RI of Microbiology MB RF, we performed clinical trials on a limited group of individuals under conditions of remote and primary vaccination to study the reactogenicity, safety and immunogenicity of the “Embryonic live recombinant variola-and-hepatitis B bivaccine, tablets (Revax-BT)”. The result of these trials were as follows:

- Rather high reactogenicity of the bivaccine at single administration especially in large doses was observed in volunteers previously vaccinated against variola (in 30% of cases) and non-vaccinated volunteers (in 50% volunteers).
- Only a large dose of the bivaccine as compared to a small one induces a protective level of VV antibodies in volunteers singly immunized under conditions of primary and remote vaccination (83% and 90%, respectively).
- Double administration of the bivaccine to volunteers (a small and a large dose) at different intervals between the administrations (1 - 2 weeks and 1, 3 - 6 months) in the maximal variant caused only slightly expressed local and general reactions.
- Only double administration of the bivaccine (a large and a small dose) at a 1 - 2 week interval created a 90 - 100% immune layer among volunteers with respect to variola, while at double administration of the bivaccine at a 1 or 3 - 6 month interval the immune layer made up 50%.
- Within not less than 6 months after double vaccination of volunteers with the bivaccine (with a large and a small dose at a 1 - 2 week interval between the administrations) the tension of VV immunity remains at a protective level as compared to a decrease observed already within 3 months after a single immunization with the preparation.
- Single and double immunizations with of volunteers with the bivaccine under conditions of primary and remote vaccination against variola did not result in the formation of a significant level of humoral immune response to HB marker (the immune layer among the vaccinated volunteers was considerably lower than 70%).
• At single and double immunizations of volunteers with the bivaccine under conditions of primary and remote vaccination (even when local and general reactions were observed in volunteers), the presence of recombinant VV in the tested blood, saliva and urine samples of volunteers was recorded in none of the cases.

Thus, an optimal scheme was found for oral immunization of volunteers against variola with the bivaccine under conditions of primary or remote vaccination including double administration of the preparation (a small and a large dose) at 1 - 2 week intervals.