VAC_24 - Thermal stability evaluation of a chimeric live-attenuated ZIKV vaccine candidate using different stabilizers in formulation

Ygara da Silva Mendes[1]; Stephanie Almeida da Silva[1]; Kelly Araújo Lúcio[1]; Mariana Pierre de Barros Gomes[1]; Noemi Rovaris Gardinali[1]; José Henrique Resende Linhares[1]; Sérgio Luiz de Lima Assumpção[1]; Sheila Maria Barbosa de Lima[1]; Renata Tourinho Santos Cantinho Bricio[1].
[1]Fiocruz/Bio-Manguinhos

Introduction: After eight years of Zika outbreak in Brazil, no vaccine has already been approved. The stability study is one of the most important steps for new vaccines development, as well as new formulations, ensuring the maintenance of product quality, safety, and efficacy throughout the shelf-life.

Objectives: So, this study aimed to evaluate the effect of excipients in different concentrations on the thermal stability of a chimeric live-attenuated Zika virus (ZIKV) vaccine to define the best formulation to be freeze-dried.

Methodology: After purification, chimeric ZIKV, produced with two concentrations of recombinant human serum albumin (rHSA), was submitted to different temperatures (2-8°C, 25°C, 37°C) for 0-14 days.

Results: It was observed that virus titers are more variable at highest temperatures. Nevertheless, the difference in residual rHSA concentration between the batches tested, 2.68–0.005 mg/mL, does not interfere in virus stability. Though, chimeric ZIKV was diluted to 10^3, 10^4 and 10^5 FFU/dose, no stabilizers, and incubated at 2- 8°C. After 4 h, the viral titer was reduced by 0.6 log to non-detectable levels (according to the test LOD), especially in most diluted conditions. Therewith, chimeric ZIKV was formulated with 10^5 FFU/dose using stabilizing excipients, generating F1, F2 and F3 solutions (minor, intermediate and major concentrations). The potency of formulated vaccines was investigated by accelerated stability assay, as previously described. It could be observed, for all tested formulations, a drop in vaccine titer from day 3 onwards, at 25°C and 37°C, excepted for control (FC), not formulated, which already loses stability at day 0. Among all tested formulations, F1 was the less stable one, losing up to 0.5-1 log FFU. Conversely, solutions F2 and F3 maintained virus stability for at least 14 days at 2-8°C. As expected, viral titers decreased as the temperature increased.

Conclusion: So, these results suggest that F2 and F3 are promising formulations to be used in the future freeze- drying tests of the ZIKV vaccine candidate. Accelerated stability tests will be repeated with the freeze-dried vaccine to determine thermal stability profile that ensures quality delivery at the point of care.

Keywords: Vaccine; ZIKV; Viral stability; Formulation