ABSTRACT

Development of a skin- and neuro-attenuated live vaccine for varicella

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ABSTRACT

Varicella caused by the primary infection of a ubiquitous neurotropic human alpha-herpesvirus, varicella-zoster virus (VZV), exerts a considerable disease burden worldwide. The current live Varicella Vaccine Strain (vOka) is generally safe and effective. However, vOka retains full ability to cause mild varicella, establish latency and reactivate to cause herpes zoster that is often clinically indistinguishable from wild-type disease in vaccine recipients. These adverse effects could be the result from vOka haplotypes carrying the disease-causing alleles, raising safety concerns. Therefore, there is a need for next-generation varicella vaccines with reduced pathogenic risk to improve the current strategy for establishing worldwide herd immunity against this disease.

Key Words: *Varicella; Disease; Vaccine*

INTRODUCTION

Here, we report a rationally-designed live varicella vaccine candidate, v7D, derived from the wild-type parental Oka strain of VZV. v7D was a pure and genetically defined VZV mutant deficient in ORF7 gene expression. This virus replicated like its parental virus in human MRC-5 fibroblasts and PBMCs (The vehicle for VZV dissemination throughout the body). However, in contrast to vOka, v7D was severely impaired for replication in human skin and neuronal cells. Meanwhile, v7D showed non-inferior immunogenicity compared with vOka in both human DC-based assays and multiple animal species, including mice, rats, guinea pigs and rabbits. Finally, v7D was proven safe and immunogenic in nonhuman primates. Our data suggest that v7D is a promising candidate as a safer live varicella vaccine and have paved the way for an ongoing first-inhuman clinical trial of v7D vaccine candidate in China.

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