Investigating live attenuated influenza vaccine efficacy in Senegal

Influenza is a highly communicable respiratory virus that poses a major infectious disease threat to populations around the world. Seasonal, or annual, influenza causes 250,000 to 500,000 deaths and up to 5 million cases of severe illness each year.[1] The emergence of a highly virulent strain could potentially kill millions of people globally.[2] Although disease burden data in the developing world are limited, available information indicates that influenza mortality and morbidity in these underserved regions are substantial and largely overlooked, with young children among the most susceptible.[3-6]

Several types of seasonal influenza vaccines are currently on the market, including live attenuated influenza vaccines (LAIVs). LAIVs have the potential to be affordable, highly effective, and viable options for young children in the developing world. They have been licensed and widely used for decades in many regions and are made using influenza virus that has been modified, or weakened, to elicit an immune response without causing influenza disease. Generally delivered through droppers or nasal spray devices, LAIVs can reduce reliance on needles and enable non-medical personnel to administer the vaccines in influenza outbreaks.

Although the best way to prevent influenza illness is through vaccination, influenza vaccines are not widely used or well-studied in tropical, low-resource countries, especially in Africa. Furthermore, available data suggest that influenza often behaves differently in tropical regions than in temperate climates. Instead of occurring in the seasonal patterns that temperate zones experience, influenza circulates year-round in some tropical regions, with one or more peaks occurring per year. In others, like in Senegal, the disease's peak does tend to be seasonal, with occurrence during the warm rainy season.[7] More research is needed to answer questions about LAIV efficacy—or the ability to prevent influenza disease—among young children in the specific context of tropical, low-resource Africa to inform the development of appropriate influenza control strategies for the region.

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EVALUATING THE BENEFITS OF LAIVS AMONG AFRICAN CHILDREN

PATH, Institut de Recherche pour le Développement, Institut Pasteur de Dakar, and the US Centers for Disease Control and Prevention (CDC) are conducting a Phase 3, double-blind, individually-randomized, placebo-controlled study to evaluate the clinical efficacy following vaccination of children in Senegal with a seasonal, trivalent LAIV candidate manufactured by the Serum Institute of India, Ltd. The LAIV candidate is formulated according to World Health Organization recommendations. It is made using the same technology as licensed LAIVs in Russia (Ultravac®) and India (NASOVAC®), and is being developed to limit cost and facilitate uptake in low-income settings.

Although previous clinical studies in India and in Bangladesh have generated data on this LAIV candidate's

safety and immunogenicity among young children and another Phase 3 efficacy study is underway in Bangladesh, this study will supplement available data by examining the LAIV candidate's efficacy among young children in a tropical, low-resource African context for the first time. Furthermore, although the influenza virus in the LAIV vaccine candidate is weakened so as not to cause disease, it must still grow in the nasal passage in order to elicit immunity to influenza. This weakened virus is adapted to grow only in the cooler temperatures of the upper respiratory tract, but vaccination prior to the influenza season in Senegal must occur during the hot, dry season when daily temperatures in much of the country are greater than 40°C. For this reason, testing the vaccine under such conditions is critical to see how the vaccine will perform and if it will be appropriate for countries like Senegal. The study will also add valuable data to the LAIV candidate's safety profile.

Following a health screening to determine eligibility and a thorough informed consent process, a total of 1,761 healthy children two through five years of age in Niakhar, Senegal, will be enrolled and vaccinated in the study and then followed for approximately six to seven months. They will be randomly selected to receive either the LAIV candidate or a placebo (inactive) vaccine. For every three study vaccinations administered, two participants will receive LAIV and one will receive placebo. Each participant will receive one 0.5 ml dose in each nostril by spray device. Participant observation will take place on a weekly basis and any children that meet referral criteria based on signs and symptoms of possible influenza or other serious illnesses will be referred to the study clinic for follow-up by a study clinician. Researchers will compare the data generated from the LAIV and placebo groups to assess vaccine efficacy and safety. They will also identify the types of influenza illness appearing and any other acute respiratory illness or fevers. In addition to this main part of the study, a subset of 100 children will also participate in a substudy that will assess if virus from the vaccine candidate is growing in the nasal passage of children receiving the active vaccine—a potential indicator that the vaccine is helping the body create immunity under the hot conditions in Senegal.

Including children down to two years of age—as opposed to the approval age of three years for the Russian and Indian LAIVs—is an important aspect of the study given the relatively high burden of disease in this age group. By providing evidence on how well this type of vaccine works among young children in Senegal, this study will help inform efforts in the scientific community to develop optimal LAIVs for the world's most vulnerable children, as well as policy decisions for potential future LAIV use in Senegal and other tropical, low-resource countries in Africa.

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