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Respiratory syncytial virus vaccine research and development: World Health Organization technological roadmap and preferred product characteristics

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ABSTRACT

The respiratory syncytial virus causes a considerable respiratory disease burden globally, most markedly in young infants, in low and middle income countries. A diverse product pipeline illustrates the recent intensification of research and development activities for vaccines and monoclonal antibodies against RSV. With the aim to ensure that product development activities are directed to address the public health needs, the World Health Organization has developed a research and development technical roadmap and articulated product characteristics preferences.

Contents

The World Health Organisation (WHO) provides guidance on vaccine research and development pathways targeting diseases of high public health interest. The respiratory syncytial virus (RSV) is responsible for a considerable respiratory disease burden, most markedly in young infants, in low and middle income countries (LMICs) [1]. Several candidate vaccines and monoclonal antibodies are currently in clinical evaluation [2]. Following a consultation process with global stakeholder, WHO developed a research and development technical roadmap and articulated product characteristics preferences [3]. The objective is to facilitate and accelerate vaccine development and guide the work of researchers, industry and funders with respect to clinical development data collection requirements, ensuring that critical, relevant public health questions are answered, supporting robust policy decision-making for licensed products to be practically implemented where most needed, without undue delays.

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The WHO strategic vision for RSV vaccines is to develop and license high-quality, safe and effective RSV vaccines that prevent severe disease and death in infants less than 12 months of age and reduce morbidity in children less than 5 years of age, and to ensure they are available and affordable for global use, including in LMICs. Two priority approaches are identified: the development of vaccines for maternal immunization during pregnancy leading to trans-placental antibody transfer and prevention of severe RSV disease in neonates and young infants, and the development of vaccines for paediatric immunization to prevent RSV disease in infants and young children.

The most severe cases occur in the first months of life. A one dose regimen administered during the second or third trimester of pregnancy, providing 70% protection against confirmed severe RSV disease in the offspring, from birth to age 4 months, was set as primary target for maternal immunization. The optimal schedule for infant vaccination will depend on whether a maternal immunization program, or monoclonal antibodies for global use against RSV, are introduced first. Protecting the most vulnerable younger children is the priority. A preferred target for paediatric vaccines was set of at least 70% vaccine efficacy against confirmed severe RSV disease over at least one-year post vaccination. HIV infection should not constitute a contra-indication to vaccination.

Vaccine efficacy against various endpoints of public health relevance, including non-severe RSV respiratory disease, should be evaluated. The long-term impact on hyper-reactive airway disease and recurrent wheezing, on health systems affected by RSV-related medical attendance and hospitalization, will be important determinants of additional vaccine value. Reduction of antibiotic use, often prescribed, for good or bad reasons, when children present with respiratory symptoms, is also an important objective.

RSV vaccine development efforts have been impeded by the legacy of a safety issue associated to the testing of a formalin-inactivated whole virus vaccine in the 1960s, which caused enhanced RSV disease (ERD) in children subsequently infected for the first time with RSV [4]. The pathogenesis of ERD is incompletely understood, and safety risk management strategies need to be developed. The risk is likely to be higher with some vaccine platforms than others [5]. The favourable safety and efficacy of first generation monoclonal antibodies for prevention of RSV-related severe adverse outcomes in high risk groups is encouraging.

The research and development roadmap highlights priority activities needed to support accelerated product availability and robust decision making when considered for regulatory licensure and policy decision. A better characterization of the vaccine-preventable disease burden is required. Epidemiological characteristics across geographical areas will inform optimal programmatic delivery planning, which could be seasonal- or age-based. Consensus, stage-gated clinical development plans should be established, to rapidly stop development of vaccines with unacceptable safety risks and to accelerate the evaluation of promising candidates. Relevant non-clinical tools (animal models, immune assays) should be standardized and openly available to support comparability studies. Vaccine evaluation must include testing in LMICs, which may require capacity strengthening of investigator networks. Building evidence on background rates of safety and efficacy endpoints, and related robust standard data collection algorithms is critical. Building manufacturing capacity to support affordable global vaccine supply will require long term planning. Collaborative planning should include developers, industry, policy makers, program delivery functions at the global, regional and national levels. When effective vaccines are on the near horizon, advocacy and communication plans will be required to strengthen awareness, mobilize resources and optimize vaccine uptake. Preparedness activities should include the strengthening of post-implementation platforms supporting vaccine impact monitoring, effectiveness and pharmacovigilance, health systems and antibiotic use.

Ethics committee approval

Not applicable.

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