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116E rotavirus vaccine development: a successful alliance

Shabir A Madhi and **Umesh D Parashar**

National Institute for Communicable Diseases, National Health Laboratory Service, Sandringham, Gauteng 2131, South Africa (SAM); Department of Science and Technology/National Research Foundation Vaccine Preventable Diseases and Medical Research Council Respiratory and Meningeal Pathogens Research Unit, University of the Witwatersrand, Johannesburg, South Africa (SAM); and Division of Viral Diseases, Centers for Disease Control and Prevention, Atlanta, GA, USA (UDP)

In *The Lancet,* Nita Bhandari and colleagues' study[1] about the efficacy of the new 116E rotavirus vaccine in Indian infants offers an opportunity to address the substantial lag in translation of scientific progress for the benefit of the world's most vulnerable population. Vaccination is considered to be second only to access to potable water in its potential cost-effectiveness as a health-care strategy for improving child health. Most childhood deaths from vaccine-preventable diseases, such as *Haemophilus influenzae* type b (Hib), *Streptococcus pneumoniae,* and rotavirus, happen in low-income countries.[2] However, introduction of lifesaving vaccines, such as Hib conjugate vaccine, into national immunisation programmes in low-income countries has lagged by as much as 20 years behind implementation in high-income settings.[3] Of the many factors responsible, constraints around vaccine affordability and supply are key.

In the past decade, progress has been made in reducing the delay in the introduction of new childhood vaccines (eg, those against pneumococcus and rotavirus) into immunisation programmes between developed and developing countries. This progress is largely attributable to international donor funding coordinated under the auspices of the GAVI Alliance, which among other things provides cofinancing for vaccine procurement at discounted prices negotiated with manufacturers for countries that meet an income threshold for eligibility (presently a gross national income per person of =US$1550). However, the sustainability of the GAVI process, in which countries are expected to take over ownership of funding for vaccine procurement once their gross national income per person exceeds GAVI's eligibility threshold, remains a concern. One way to address this challenge is to explore approaches to development of low-cost, safe, and effective vaccines that are affordable for low-income countries.

Correspondence to: Shabir A Madhi.

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Within this framework, the development of 116E rotavirus vaccine provides a model of a successful tripartite alliance between donors, governmental institutions, and a willing private sector, to ensure that vaccines are developed at affordable prices. Clinical development of the 116E vaccine was undertaken by an emerging Indian vaccine manufacturer—Bharat Biotech—with full partnership and partial financial support from the Department of Biotechnology of the Indian Government, and with technical and financial support from a consortium of international partners and donors. In lieu of public sector support to offset some of the research and development costs, the manufacturer has committed to making the vaccine available to the public sector at less than $1 per dose for a three-dose series. This regime is in comparison to the discounted cost, $2·50 per dose for a two-dose series and $3·50 per dose for a three-dose series, of two other licensed rotavirus vaccines that GAVI pays for countries that procure vaccine through UNICEF.[4] Beneficiary low-income countries contribute $0·40 in co-financing for a full series of either vaccine.[5]

In Bhandari and colleagues' study,[1] which included more than 6500 infants aged 6–7 weeks in urban and rural settings, overall efficacy of the 116E vaccine against severe rotavirus gastroenteritis was 53·6% (95% CI 35·0–66·9). Efficacy during the first year of life was 56·4% (36·6–70·1), which is similar to that of the two other licensed rotavirus vaccines in developing country settings: 50% (19–68) in Malawi for the monovalent rotavirus vaccine, and 46% (–1 to 72) in Bangladesh and 64% (40–79) in low-income African countries for the pentavalent rotavirus vaccine.[6–8] The similar efficacy of 116E against severe rotavirus gastroenteritis caused by non-vaccine-type strains in post-hoc analysis is particularly reassuring in view of some concern that the unusual G9P[11] rotavirus strain in the 116E vaccine might protect less well against non-vaccine-type strains that cause most cases of severe disease in children in India and globally.[9] Similar heterotypic protection has also been reported with the monovalent human-derived G1P[8] vaccine, and after natural rotavirus infection.[10,11]

Although a vaccine efficacy of 50–60% seems to be modest, on the basis of the tremendous health burden of severe rotavirus gastroenteritis in India and other low-income countries, even a vaccine with modest efficacy will have substantial public health benefit. Reassuringly, 116E vaccine was not linked with intussusception—an adverse event that has been associated with other rotavirus vaccines in some settings. However, Bhandari and colleagues' trial was inadequately powered to detect a low risk of adverse events, and

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postmarketing efforts to monitor intussusception should continue. Furthermore, any risks identified should be weighed against the large anticipated benefits from vaccination.[12]

The successful testing and impending licensure of the 116E vaccine, followed by its potential inclusion into the national immunisation programme of India, represents a major milestone in global efforts to reduce rotavirus-associated morbidity and mortality in India, the country which singularly accounts for about a fifth of global deaths from rotavirus.[13] Should the vaccine be prequalified by WHO, it will provide an additional affordable product to meet the large demand of the global market. The public–private sector partnership to develop and test the vaccine (somewhat similar to the approach used to develop a new meningitis vaccine, MenAfriVac, that is already realising a huge public health effect in Africa) provides an alternative model of risk and cost sharing to develop life-saving vaccines that are effective, safe, and affordable for use in low-income countries.

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References

1. Bhandari, N., Rongsen-Chandola, T., Bavdekar, A., et al. for the India Rotavirus Vaccine Group. Efficacy of a monovalent human-bovine (116E) rotavirus vaccine in Indian infants: a randomised, double-blind, placebo-controlled trial. Lancet. 2014. published online March 12. http://dx.doi.org/10.1016/S0140-6736(13)62630-6
2. Lozano R, Naghavi M, Foreman K, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet. 2012; 380:2095–128. [PubMed: 23245604]
3. Levine OS, Hajjeh R, Wecker J, et al. A policy framework for accelerating adoption of new vaccines. Hum Vaccin. 2010; 6:1021–24. [PubMed: 21150269]
4. Unite for Children. [accessed Dec 7, 2013] UNICEF procurement prices for rotavirus vaccines. Jul 30. 2013 http://www.unicef.org/supply/files/Rotavaccine.pdf
5. GAVI Alliance. [accessed Dec 7, 2013] Vaccine co-financing: frequently asked questions. Jun. 2013 http://www.gavialliance.org/library/documents/gavi-documents/guidelines-and-forms/vaccine-co-financing-faqs/
6. Madhi SA, Cunliffe NA, Steele D, et al. Effect of human rotavirus vaccine on severe diarrhea in African infants. N Engl J Med. 2010; 362:289–98. [PubMed: 20107214]
7. Armah GE, Sow SO, Breiman RF, et al. Efficacy of pentavalent rotavirus vaccine against severe rotavirus gastroenteritis in infants in developing countries in sub-Saharan Africa: a randomised, double-blind, placebo-controlled trial. Lancet. 2010; 376:606–14. [PubMed: 20692030]
8. Zaman K, Dang DA, Victor JC, et al. Efficacy of pentavalent rotavirus vaccine against severe rotavirus gastroenteritis in infants in developing countries in Asia: a randomised, double-blind, placebo-controlled trial. Lancet. 2010; 376:615–23. [PubMed: 20692031]
9. Bányai K, László B, Duque J, et al. Systematic review of regional and temporal trends in global rotavirus strain diversity in the pre rotavirus vaccine era: insights for understanding the impact of rotavirus vaccination programs. Vaccine. 2012; 30:A122–30. [PubMed: 22520121]
10. Patel MM, Glass R, Desai R, Tate JE, Parashar UD. Fulfilling the promise of rotavirus vaccines: how far have we come since licensure? Lancet Infect Dis. 2012; 12:561–70. [PubMed: 22742639]
11. Velazquez FR, Matson DO, Calva JJ, et al. Rotavirus infections in infants as protection against subsequent infections. N Engl J Med. 1996; 335:1022–28. [PubMed: 8793926]

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12. Parashar UD, Orenstein WA. Intussusception and rotavirus vaccination—balancing risk against benefit. Clin Infect Dis. 2013; 57:1435–37. [PubMed: 23964087]

13. Tate JE, Burton AH, Boschi-Pinto C, et al. 2008 estimate of worldwide rotavirus-associated mortality in children younger than 5 years before the introduction of universal rotavirus vaccination programmes: a systematic review and meta-analysis. Lancet Infect Dis. 2012; 12:136–41. [PubMed: 22030330]