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ROTAVIRUS VACCINE FOR NEONATES

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COMMENTARY

Rotavirus is a leading cause of morbidity and mortality for neonates and children. Worldwide, over 200,000 children die from rotavirus gastroenteritis each year (1) and more than 90 million infants still lack access to a rotavirus vaccine (2). Traditional vaccine schedules administer doses at 8 weeks, 14 weeks and 18 weeks of age. Therefore, neonates are often exposed to rotavirus before the first dose is given (3). This is of particular importance in low income countries, where access to vaccine is poor, there is earlier onset of rotavirus disease and the burden of disease significant (4).

Current vaccines approved for use are *Rotarix*™ (GSK Vaccines, Wavre, Belgium) and *RotaTeq*™ (Merck & Co, Kenilworth, USA). These have not been investigated with a neonatal dosing schedule. Furthermore, there is evidence of suboptimal vaccine efficacy in low- and middle-income countries (5).

RV3-BB is a novel vaccine which has been investigated in early phase trials in Australia (6) and New Zealand (7). It is developed from a human rotavirus strain, RV3 (G3P[6]) found in infants with asymptomatic infection. Dosing at birth is likely to be efficacious and safe: RV3-

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BB P[6] vaccine strains effectively adhere to the newborn gut (8), display minimal interference from maternal breast milk (9) and are naturally attenuated (2). This strain also provides heterotypic serologic responses, which may offer cross-protection against other circulating rotavirus strains (2). Further potential advantages of a neonatal schedule include improved uptake, particularly in low-income countries.

This randomised, double-blind, placebo-controlled trial in Indonesia demonstrated the efficacy of a human neonatal rotavirus vaccine in preventing severe rotavirus gastroenteritis before 18 months of age. When administered on a neonatal dosing schedule, RV3-BB had a vaccine efficacy of 94% at 12 months of age and 75% at 18 months of age. RV3-BB administered on both the neonatal and infant schedules demonstrated comparable or superior efficacy to other rotavirus vaccines in low-income countries (2). While the trial was underpowered to detect rare adverse events, no cases of intussusception were detected within 21 days of vaccine administration. Only one participant in the trial developed intussusception in the infant-schedule arm; at 8.5 months of age, 114 days after the third dose of vaccine.

The authors chose a one-sided alpha level of 0.1. It is unclear why this unconventional significance level was chosen, perhaps in order to limit the sample size required for the trial. Nevertheless, the results obtained for the primary outcome and vaccine efficacy had far lower p values than this, therefore the interpretation of the results is unchanged.

This is a large study with rigorous methodology that demonstrates the efficacy of a new human rotavirus vaccine in a low-income country with high burden of disease. While the benefits of a neonatal schedule are clear in this setting, the applicability to other settings with higher vaccine coverage is unknown. Furthermore, there has not been a direct comparison of this rotavirus vaccine with the other vaccines currently in use. Nevertheless, this vaccine shows promise for addressing the ongoing global burden of rotavirus disease.

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CONFLICT OF INTEREST

None

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