Letter to the Editor on Cross-Protection of RotaTeq

Ma et al estimated the effectiveness of RotaTeq™ (pentavalent rotavirus vaccine, RV5), containing human bovine reassortants G1, G2, G3, G4, and P[8], against rotavirus gastroenteritis at 97% (95% CI, 83%-100%) in a cohort of children (14 weeks to 2 years of age) predominantly infected (79%) with G8P[8], in Shanghai, China.[1] RV5 has been shown to be efficacious and effective across geographic settings, time-periods, and strains, but protection of RV5 against a G8 strain had been demonstrated previously only in Africa.[2-6]

Cross-protective effects are seen for rotavirus vaccines.[7,8] RV5's broad, cross-protective effects are consistent with immunologic studies showing that its pentavalent three-dose formulation elicits a higher magnitude and longer duration of immunologic response than other rotavirus vaccines.[9-11] Two previous meta-analyses have shown that protection from RV5 against homotypic (matched the G- and P-types of the vaccine) and partially heterotypic (matched only one of the G- or P-types) strains was similar.[12,13] Of note, clinical and postlicensure studies show that Rotarix (monovalent formulation) may be marginally less effective against the fully heterotypic G2P[4] genotype.[14-18] Notably, fully heterotypic strains to RV5 are rare globally, due to its pentavalent, human-bovine reassorted formulation.[19-21] In Europe, where large scale strain surveillance started in 2007, fully heterotypic strains to RV5 were detected in only 1% of typed samples (considering all strains circulating at ≥1% prevalence).[22] The assessment of protection in clinical trials and observational studies against specific strains can be made only against the strains circulating during the study period. As this is unpredictable, achieving statistical power to demonstrate the quantitative level of protection against rarer strains is challenging in clinical and observational studies. Despite this, high protection of RV5 against the fully heterotypic G8P[6] strain has been demonstrated.[2,3]

Ma et al provide evidence of similar, high protection of RV5 against G8P[8], a partially heterotypic strain, outside Africa and, thus, advanced new estimates that are aligned with previous knowledge of the broad cross-protective effects of RotaTeq™.[1]

CRediT Authorship Contribution Statement

Cristina Carias: Conceptualization, Writing – original draft, Writing – review & editing. **Susanne Hartwig:** Writing – original draft, Writing – review & editing, Conceptualization. **Nabi Kanibir:** Writing – review & editing, Conceptualization, Writing – original draft. **Jelle Matthijnssens:** Writing – review & editing, Conceptualization. **Yingmei Tu:** Writing – review & editing, Conceptualization, Writing – original draft.

Declaration of Competing Interest

Cristina Carias, Susanne Hartwig, Nabi Kanibir, and Yingmei Tu are employees of Merck & Co., Inc., Rahway, NJ, USA, a manufacturer of RotaTeq™. Jelle Matthijnssens has received consulting fees from GlaxoSmithKline and Merck & Co., Inc., Rahway, NJ, USA.

Cristina Carias, PhD
Merck & Co., Inc., Rahway, New Jersey

Susanne Hartwig, PharmD
MSD France, Lyon, France

Nabi Kanibir, MD
Global Medical and Scientific Affairs, MSD International GmbH Luzern, Switzerland

Jelle Matthijnssens, PhD
Department of Microbiology and Immunology, Laboratory of Viral Metagenomics, Rega Research Institute for Medical Research, University of Leuven, Leuven, Belgium

Yingmei Tu, MD
Merck & Co., Inc., Rahway, New Jersey

https://doi.org/10.1016/j.jpeds.2024.113952

References

1. Ma W, Wei Z, Guo J, Lu L, Li J, Cai J, et al. Effectiveness of pentavalent rotavirus vaccine in Shanghai, China: a test-negative design study. J Pediatr 2023;259:113461.
2. Heylen E, Zeller M, Ciarlet M, Lawrence J, Steele D, Van Ranst M, et al. Comparative analysis of pentavalent rotavirus vaccine strains and G8 rotaviruses identified during vaccine trial in Africa. Sci Rep 2015;5:14658.
3. Breiman RF, Zaman K, Armah G, Sow SO, Anh DD, Victor JC, et al. Analyses of health outcomes from the 5 sites participating in the Africa and Asia clinical efficacy trials of the oral pentavalent rotavirus vaccine. Vaccine 2012;30:A24-9.
4. Burnett E, Parashar UD, Tate JE. Real-world effectiveness of rotavirus vaccines, 2006–19: a literature review and meta-analysis. Lancet Glob Health 2020;8:e1195-202.
5. Bergman H, Henschke N, Hungerford D, Pitan F, Ndwandwe D, Cunliffe N, et al. Vaccines for preventing rotavirus diarrhoea: vaccines in use. Cochrane Database Syst Rev 2021:CD008521.
6. Soares-Weiser K, Bergman H, Henschke N, Pitan F, Cunliffe N. Vaccines for preventing rotavirus diarrhoea: vaccines in use. Cochrane Database Syst Rev 2019:CD008521.
7. Leshem E, Parashar U. Use of surveillance data to assess the Impact of vaccination on circulating rotavirus strains. J Pediatric Infect Dis Soc 2015;4:e90-2.
8. RotaCouncil. The impact of rotavirus vaccination; 2022. Accessed March 7, 2024. https://preventrotavirus.org/wp-content/uploads/2022/09/ROTA-Brief7-VaccineImpact2022.pdf
9. Diller JR, Carter MH, Kanai Y, Sanchez SV, Kobayashi T, Ogden KM. Monoreassortant rotaviruses of multiple G types are differentially neutralized by sera from infants vaccinated with ROTARIX and RotaTeq. J Infect Dis 2021;224:1720-9.

10. Velasquez-Portocarrero DE, Wang X, Cortese MM, Snider CJ, Anand A, Costantini VP, et al. Head-to-head comparison of the immunogenicity of RotaTeq and Rotarix rotavirus vaccines and factors associated with seroresponse in infants in Bangladesh: a randomised, controlled, open-label, parallel, phase 4 trial. Lancet Infect Dis 2022;22:1606-16.
11. Angel J, Franco MA, Greenberg HB. Rotavirus immune responses and correlates of protection. Curr Opin Virol 2012;2:419-25.
12. Leshem E, Lopman B, Glass R, Gentsch J, Bányai K, Parashar U, et al. Distribution of rotavirus strains and strain-specific effectiveness of the rotavirus vaccine after its introduction: a systematic review and meta-analysis. Lancet Infect Dis 2014;14:847-56.
13. Cates JE, Amin AB, Tate JE, Lopman B, Parashar U. Do rotavirus strains affect vaccine effectiveness? A systematic review and meta-analysis. Pediatric Infect Dis J 2021;40:1135.
14. Middleton BF, Danchin M, Quinn H, Ralph AP, Pingault N, Jones M, et al. Retrospective case-control study of 2017 G2P [4] rotavirus epidemic in rural and remote Australia. Pathogens 2020;9:790.
15. Snelling T, Andrews R, Kirkwood C, Culvenor S, Carapetis J. Case-control evaluation of the effectiveness of the G1P [8] human rotavirus vaccine during an outbreak of rotavirus G2P [4] infection in central Australia. Clin Infect Dis 2011;52:191-9.
16. Correia JB, Patel MM, Nakagomi O, Montenegro FM, Germano EM, Correia NB, et al. Effectiveness of monovalent rotavirus vaccine (Rotarix) against severe diarrhea caused by serotypically unrelated G2P [4] strains in Brazil. J Infect Dis 2010;201:363-9.
17. Amin AB, Cates JE, Liu Z, Wu J, Ali I, Rodriguez A, et al. Rotavirus genotypes in the post-vaccine era: a systematic review and meta-analysis of global, regional, and temporal trends in settings with and without rotavirus vaccine introduction. J Infect Dis 2023:1-10. https://doi.org/10.1093/infdis/jiad40
18. Amin AB, Tate JE, Waller LA, Lash TL, Lopman BA. Monovalent rotavirus vaccine efficacy against different rotavirus genotypes: a pooled analysis of phase II and III trial data. Clin Infect Dis 2022;76:e1150-6.
19. Dóró R, László B, Martella V, Leshem E, Gentsch J, Parashar U, et al. Review of global rotavirus strain prevalence data from six years post vaccine licensure surveillance: is there evidence of strain selection from vaccine pressure? Infect Genet Evol 2014;28:446-61.
20. Degiuseppe JI, Stupka JA. Genotype distribution of Group A rotavirus in children before and after massive vaccination in Latin America and the Caribbean: systematic review. Vaccine 2020;38:733-40.
21. Matthijnssens J, Joelsson DB, Warakomski DJ, Zhou T, Mathis PK, van Maanen MH, et al. Molecular and biological characterization of the 5 human-bovine rotavirus (WC3)-based reassortant strains of the pentavalent rotavirus vaccine. RotaTeq. Virology 2010;403:111-27.
22. EuroRotanet annual report 2021. European Rotavirus Network; 2023. Accessed March 7, 2024. https://www.eurorotanet.com/project-information/documents-and-methods/