Effectiveness of monovalent rotavirus vaccine against hospitalization with acute rotavirus gastroenteritis in Kenyan children

Khagayi S¹, Omore R¹, Audi A¹, Ogwel B¹, Ochieng B¹, Juma J¹, Apondi E¹, Bigogo G¹, Onyango C³, Ngama M², Otieno G², Njeru R², Owor BE², Mwanga MJ², Tuck B³, Addo Y³, Breiman RF³, Tabu C⁴, Amwayi A⁴, Mwenda JM⁶, Tate JE⁷, Parashar UD⁷, Nokes DJ², Verani JR⁸

Affiliations
¹Kenya Medical Research Institute (KEMRI)-Centre for Global Health Research (CGHR), Kisumu, Kenya;
²Centres for Disease Control and Prevention, Kisumu, Kenya
³KEMRI-Centre for Geographic Medicine Research-Coast (CGMRC)/KEMRI-Wellcome Trust Research Programme, Kilifi, Kenya;
⁴Emory Global Health Institute (EGHI), Emory University, Atlanta, GA, USA;
⁵Ministry of Health, Nairobi, Kenya;
⁶WHO Regional Office for Africa (WHO/AFRO), Brazzaville, Republic of Congo;
⁷Viral Gastroenteritis Branch, Division of Viral Diseases, Centers for Disease Control and Prevention (CDC), Atlanta, GA, USA;
⁸School of Life Sciences and Zeeman Institute for Systems Biology and Infectious Disease Epidemiology Research (SBIDER), University of Warwick, UK
⁹Centers for Disease Control and Prevention, Nairobi, Kenya

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July 30- August 10, 2019
In Kenya, before rotavirus vaccine introduction, among <5 yr olds, rotavirus responsible;
  - 19% (~9,000) of all hospitalizations with diarrhea
  - 16% (~1.5 million) of all clinic visits
  - > 4,000 deaths a leading cause of severe diarrhea

Kenya introduced monovalent rotavirus vaccine (RV1) in July 2014

Rotavirus Immunization Program Evaluation in Kenya (RIPEK) established among institutions with rotavirus disease surveillance platforms
  - Evaluate effectiveness of RV1 against rotavirus diarhoea hospitalization in children <5 years of age in Kenya
Methods

• Children <5 years hospitalized with gastroenteritis at participating facility between July 2014 and Dec 2017 enrolled

• Eligible to have received ≥1 dose of rotavirus vaccine
  – ≥ 8 weeks of age and born 6 weeks before date of vaccine introduction (24th April 2014) or later

• Provided stool specimen for rotavirus testing by ELISA

• Card/registry confirmed vaccination history
  – Dose of rotavirus vaccine considered valid (i.e. immunologically protective) if administered >14 days before admission date
Methods

• Case control vaccine-effectiveness using ‘Test negative’ design
  – **Cases**: rotavirus-positive
  – **Controls**: rotavirus-negative

• Compare vaccination coverage among cases and controls
  • Calculate odds ratio (OR) for RV1 vaccination
  • Adjusted for age in weeks and
  • Assessed for other potential confounders including variables in age/date/site-adjusted model

• Vaccine effectiveness = 1-OR x100%
Results
Enrolled participants

All age eligible: 677

- Controls: 567 (84%)
  - Vaccination data: 418 (74%)
    - 0 doses: 69 (16%)
    - 1 dose: 41 (10%)
    - 2 doses: 308 (74%)
  - No vaccination data: 149 (26%)
- Cases: 110 (16%)
  - Vaccination data: 91 (83%)
    - 0 doses: 33 (36%)
    - 1 dose: 7 (8%)
    - 2 doses: 51 (56%)
  - No vaccination data: 19 (17%)
Enrolled participants

All age eligible
677

Controls
567 (84%)

Vaccination data
418 (74%)

0 doses
69 (16%)

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2 doses
308 (74%)

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## Vaccine effectiveness estimates

<table>
<thead>
<tr>
<th>Dosage</th>
<th>% Vaccinated</th>
<th>Adjusted* VE (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases (N=91)</td>
<td>Controls (N=418)</td>
</tr>
<tr>
<td>2 doses</td>
<td>51/83 (61%)</td>
<td>308/365 (84%)</td>
</tr>
<tr>
<td>≥1 doses</td>
<td>58/91 (64%)</td>
<td>349/418 (83%)</td>
</tr>
</tbody>
</table>

*Adjusted for age in weeks, date of enrollment and site*
## Vaccine effectiveness estimates

<table>
<thead>
<tr>
<th>Age group</th>
<th>% Vaccinated</th>
<th>Adjusted* VE (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases (N=91)</td>
<td>Controls (N=418)</td>
</tr>
<tr>
<td>&lt;12 months</td>
<td>33/55 (60%)</td>
<td>184/218 (84%)</td>
</tr>
<tr>
<td>≥12 months</td>
<td>18/28 (64%)</td>
<td>124/147 (84%)</td>
</tr>
</tbody>
</table>

*Adjusted for age in weeks, date of enrollment and site
### Vaccine effectiveness estimates

<table>
<thead>
<tr>
<th>Study site</th>
<th>% Vaccinated</th>
<th>Adjusted* VE (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases (N=91)</td>
<td>Controls (N=418)</td>
</tr>
<tr>
<td>Kilifi</td>
<td>33/58 (57%)</td>
<td>192/237 (81%)</td>
</tr>
<tr>
<td>Siaya</td>
<td>7/14 (47%)</td>
<td>58/67 (79%)</td>
</tr>
<tr>
<td>Lwak</td>
<td>11/11 (100%)</td>
<td>58/61 (95%)</td>
</tr>
</tbody>
</table>

*Adjusted for age in weeks, date of enrollment and site
Vaccine effectiveness estimates

<table>
<thead>
<tr>
<th>Disease severity (20 point Vesikari score)</th>
<th>% Vaccinated</th>
<th>Adjusted* VE (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases (N=91)</td>
<td>Controls (N=418)</td>
</tr>
<tr>
<td>Less severe</td>
<td>34/53 (64%)</td>
<td>206/240 (86%)</td>
</tr>
<tr>
<td>Severe</td>
<td>17/30 (55%)</td>
<td>102/125 (82%)</td>
</tr>
</tbody>
</table>

*Adjusted for age in weeks, date of enrollment and site
<table>
<thead>
<tr>
<th>Nutrition status</th>
<th>% Vaccinated</th>
<th>Adjusted* VE (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases (N=91)</td>
<td>Controls (N=418)</td>
</tr>
<tr>
<td>Weight for age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal (z score ≥ -2)</td>
<td>28/51 (55%)</td>
<td>184/210 (87%)</td>
</tr>
<tr>
<td>z score &lt;-2</td>
<td>22/31 (70%)</td>
<td>122/152 (80%)</td>
</tr>
<tr>
<td>Height for age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>33/58 (57%)</td>
<td>210/247 (85%)</td>
</tr>
<tr>
<td>z score &lt;-2</td>
<td>17/23 (74%)</td>
<td>98/118 (83%)</td>
</tr>
<tr>
<td>Weight for height</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>31/57 (54%)</td>
<td>192/218 (88%)</td>
</tr>
<tr>
<td>z score &lt;-2</td>
<td>19/25 (76%)</td>
<td>112/142 (79%)</td>
</tr>
</tbody>
</table>

*Adjusted for age in weeks, date of enrollment and site
<table>
<thead>
<tr>
<th>Genotypes</th>
<th>% Vaccinated</th>
<th>Adjusted** VE (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases (N=91)</td>
<td>Controls (N=418)</td>
</tr>
<tr>
<td>α</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G1P[8]</td>
<td>13/32 (41%)</td>
<td>308/365 (84%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>60% (3% to 83%)</td>
</tr>
<tr>
<td>G2P[4]</td>
<td>15/18 (83)</td>
<td>308/365 (83%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>29% (-184% to 82%)</td>
</tr>
</tbody>
</table>

*Adjusted for age in weeks, date of enrollment and site
RV1 offers significant protection against rotavirus associated hospitalization
  – Consistent with data emerging from other African countries

Significant effectiveness among well-nourished children, but not for underweight, stunted or wasted
  – May explain, in part, lower efficacy and effectiveness in low- and middle-income countries compared to high-income settings
  – Kilfi with a lower effectiveness (63%) compared to Siaya (81%) also had higher levels of malnutrition
Discussion

• Observed similar levels of protection among children <12 and ≥12 months
  • Protection extends to second year of life

• Point estimate of VE against G1P[8] was significant for but not for G2P[4]
  • Limited statistical power; important to monitor circulating strains post-introduction
Limitations

• Exclusion of 17% of cases and 26% of controls due to lack of card-confirmed vaccination data

• Included only three sites, two of which are located in the same region; may affect generalizability

• Genotype data only available for a subset of cases, limiting our ability to examine strain-specific VE
Thank you!

For more information please contact:

KEMRI CGHR
P.O. Box 1578
Kisumu, Kenya
E-mail: info@kemricdc.org

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the KEMRI Center for Global Health Research.