HIV-1 Vaccine Induced Antibodies: Infants vs. Adults

845

[1,2]Nonhlanhla N Mkhize, [3]Jack Heptinstall, [3]Lu Zhang, [4]Shiyu Chen, [1,2]Haajira Kaldine, [1,2]Prudence Kgagudi, [4]Amanda S Woodward Davis, [3]Derrick Goodman, [5]Robert Parks, [3]Kelly E Seaton, [4]K. Rachael Parks, [1,2]Penny L Moore, [6]James Kobie, [7]Magdalena E Sobieszczyk, [8]Genevieve Fouda, [9]Kinga K. Smolen, [9]Ofer Levy, [5]Barton F. Haynes, [5]David Montefiori, [10]Glenda Gray, [11]William O. Hahn, [10]Avy Violari, [3]Guido Ferrari, [4]Lawrence Corey, [4]Holly Janes and [3]**Georgia D. Tomaras**

1SAMRC Antibody Immunity Research Unit, University of the Witwatersrand, 2National Institute for Communicable Diseases of the National Health Laboratory Service, Johannesburg, South Africa, 3Center for Human Systems Immunology, Departments of Surgery and Integrative Immunobiology, Duke University, Durham, NC 27701, USA, 4Vaccine and Infectious Disease Division, Fred Hutchinson Cancer Center, Seattle, WA, USA, 5Duke Human Vaccine Institute, Duke University School of Medicine, Durham NC 27710 USA, 6University of Birmingham at Alabama, Birmingham, AL, USA, 7Department of Medicine, Division of Infectious Diseases, Columbia Vagelos College of Physicians and Surgeons, New York, NY, USA, 8Weill Cornell, New York, New York, USA, 9Precision Vaccines Program, Boston Children's Hospital; Boston, MA, USA; Harvard Medical School; Boston, MA, USA, 10University of the Witwatersrand, Perinatal HIV Research Unit, Faculty of Health Sciences, Johannesburg, South Africa; South African Medical Research Council, Cape Town, South Africa, 11 University of Washington, Department of Medicine, Division of Allergy and Infectious Disease, Seattle; Fred Hutchinson Cancer Center, Seattle WA, USA

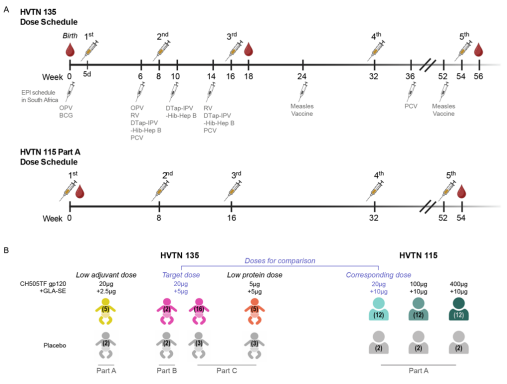
BACKGROUND

- Broadly neutralizing antibodies (bnAbs) can prevent HIV acquisition but are challenging to elicit by vaccination.
- Infants living with HIV more readily develop bnAbs, raising the hypothesis that vaccine-induced bnAbs may be more easily generated in infants.
- This study investigates the induction of antibody (Ab) responses in infants vaccinated with CH505TF gp120 and evaluates how these responses compare to adults who received the same vaccine regimen

METHODS

- Samples
  - Serum and PBMCs from infants born to mothers living with HIV (HVTN 135 in **South Africa**) and healthy adults (HVTN 115 in the **US**) received five doses of 20µg of a clade C gp120, CH505TF, with GLA-SE on a harmonized vaccination schedule.

HVTN 115 and HVTN 135 vaccination schedules and study groups.



A) HVTN 135 schedule of infant immunizations and blood draws in relation to standard infant immunizations, and HVTN 115 adult immunization schedule and blood draws; B) Schema for HVTN 135 and HVTN 115 Part A.

- Assays
  - At baseline and 2 weeks post-5th vaccination (Week 56)
  - BAMA, B-cell phenotyping
  - ADCC and ADCP
  - TZM-bl neutralizing antibody assay.
  - Pediatric Vaccine Multiplex Assay to assess Ab responses to routine childhood vaccines (HiB, HepB, Diphtheria, Tetanus and Pertussis).

Given the same vaccine regimen, with harmonised immune assessments, infants elicited immune responses with a magnitude and quality that were comparable to or higher than adults, especially neutralizing antibodies and FcR binding

RESULTS

1. Decline of gp41 IgG at week 56 indicates waning maternal Abs in Infants

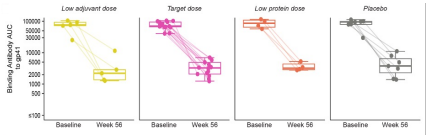


Figure 1. IgG gp41-specific binding Abs at baseline and Week 56 in each treatment group

2. All infant vaccine recipients demonstrated high Tier 1A neutralization, IgG binding responses to CH505 gp120 and high levels of CH505+ B cells

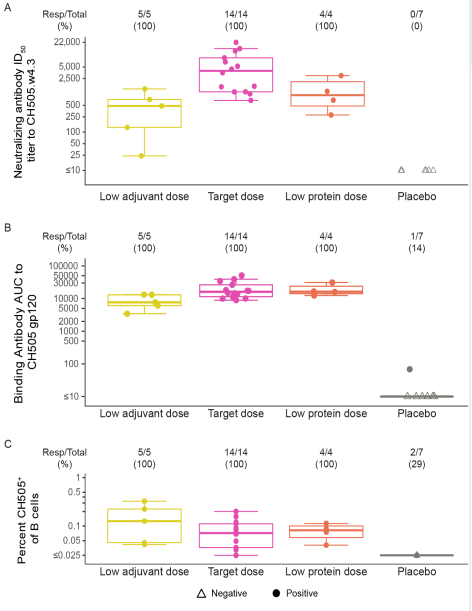


Figure 2. A) Neutralizing antibody ID50 titer to the Tier 1A vaccine strain, CH505.w4.3, by TZM-bl assay; B) IgG binding Ab responses to the vaccine-matched CH505TF gp120 by BAMA; C) B cell phenotyping measured by percent of B cells that are CH505+ by flow cytometry.

3. Vaccine-induced ADCP function increases while ADCC is similar between placebo and vaccinated infants two weeks post-last vaccination

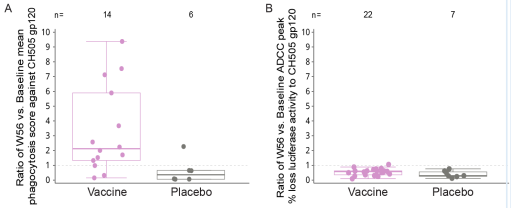


Figure 3. Ratio of Week 56 vs. Baseline ADCP function against the vaccine-matched CH505TF gp120 as measured by mean phagocytosis score, by BAMA. B) Ratio of Week 56 vs. Baseline ADCC function against the vaccine-matched CH505TF gp120 as measured by peak percent loss luciferase, by ADCC luciferase assay.

4. CH505-specific humoral immune responses two weeks post-last vaccination are higher in infants (HVTN 135) than adults (HVTN 115)

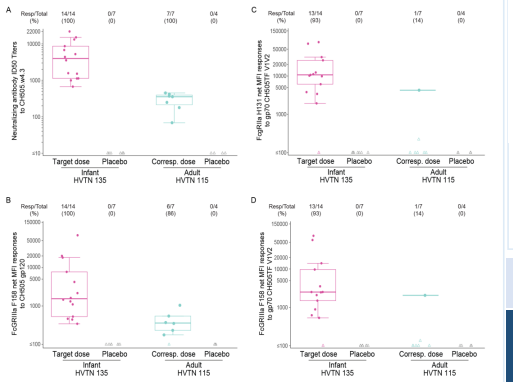


Figure 4. A) Neutralizing antibody ID50 titer to the tier 1A vaccine strain, CH505.w4.3, by TZM-bl assay. B) FcγRIIIa F158 responses to the vaccine-matched CH505TF gp120 by BAMA. C) FcγRIIa H131 responses to the vaccine-matched CH505TF gp70 by BAMA. D) FcγRIIIa F158 responses to the vaccine-matched CH505TF gp70 by BAMA

Acknowledgements

The team acknowledges the stellar work of the staff at the PHRU Clinical Research Site. Without the participation of the infants and their caregivers this study would not have been possible. We thank the laboratory scientists and data analysts and the HVTN 135 protocol team. The trial was funded through National Institute of Allergy and Infectious Disease of the National Institutes of Health under Grants UM1 AI068614 [HVTN Leadership and Operations Center], UM1 AI068635 [HVTN Statistical and Data Management Center], and UM1 AI068618 [HVTN Laboratory Center]

RESULTS

5. Summary of comparison of CH505 vaccine-induced immune responses for adults in HVTN 115 and infants in HVTN 135

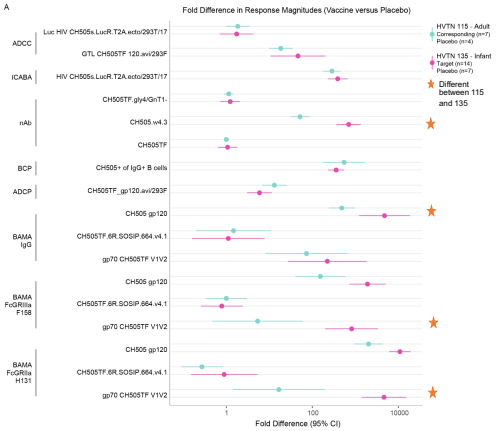


Figure 5. A) Forest plot comparing magnitude of vaccine effects, i.e. fold differences vaccine vs. placebo, for CH505 antigen-specific immune responses in adults vs. infants; B) Radar plot comparing rates of epitope-specific immune responses in CH505-vaccinated adults vs infants. Orange stars denote functions that demonstrated differences between placebo and vaccinated

CONCLUSIONS

- Maternal Abs did not interfere with vaccine humoral immunogenicity in infants and the vaccine did not alter infant humoral responses to childhood vaccinations
- Given the same vaccine, infants elicited similar or higher immune responses compared to adults
- These results indicate potential improvements in the quality of Abs elicited early in life and support continued investigation of HIV vaccines in infants.