expressed in whole blood from the different vaccine dose groups. Linear Regression analysis was used to correlate gene expression with ICS data. Statistical Inference was assessed using Wilcoxon rank sum test.
Results: DCVax induced greater IFN gene expression and IL-12 production in whole blood compared to polyICLC alone, and in a dose-dependent fashion that correlated with PRDM1(BLIMP1) expression in CD4 cells and total Gag-specific CD4 TH1 and CD8 IFNγ producing T cells in the high dose vaccinees. Pathway analysis on top regression features showed differential proinflammatory responses (e.g. IL1, RXR, LPS) at 1 d in subjects that mounted potent Gag-specific CD4 responses. High dose subjects upregulated genes downstream of IL-1R signaling (e.g. IRAK3, MAPK2K3) including NF-κB. Gag-specific CD4 TH1 responses correlated with IL1R, WNT, and γ-C receptor cytokine signaling pathways that might also predispose toward greater CD4 T cell memory development.
Conclusions: Synergy was seen with the high dose HIV Gag p24 dendritic cell targeted vaccine and polyICLC for induction of both a quantitative and qualitative greater Type I IFN response compared to lower vaccine doses or polyICLC alone. This resulted in optimum CD4 TH1 and CD8 CTL responses. Of note, only the high dose and polyICLC combination induced SOCS-1, a critical regulator of type I interferon signaling. These results highlight that combinations of vaccine and adjuvant can trigger quantitatively different responses.

Participation in Trials: Willingness, Benefits and Challenges

P42.01
Self-reported Benefits of Study Participation in HVTN 503, ''Phambili''

Mary A. Allen[1], Barbara Metch[2], Zoe Moodie[2], Linda-Gail Bekker[3], Gavin Churchyard[4], Koleka Mlisana[5], Maphoshane Nchabeleng[6], Jim Kublin[2], Glenda Gray[7], HVTN 503 Study Team

[1]NIH/NIAID, DAIDS, Bethesda, MD, United States, [2]FHCRC, Seattle, WA, United States, [3]Desmond Tutu HIV Foundation, Cape Town, South Africa, [4]Aurum Institute, Klerksdorp, South Africa, [5]University of KwaZulu Natal, Durban, South Africa, [6]Medunsa Clinical Research Unit, Medunsa, South Africa, [7]Chris Hani Baragwanath Hospital, PHRU, Soweto, South Africa

Background: Participants (ppts) in HVTN 503 (''Phambili''), the only HIV vaccine efficacy trial conducted in Africa to date, were asked about possible benefits of study participation.
Methods: Social impact (SI) assessment was conducted at weeks 12, 78, 130, and 182, and included asking ''In the last 6 months, has participation in this study had a beneficial impact on your life?'' Benefits were analyzed by sex, age, study site and treatment group.
Results: Of the 801 ppts enrolled, 752 (94%) reported that study participation had a beneficial impact on their lives, and only 48 (6%) reported negative social impacts (NSI). Overall, 705 (88.0%) reported a benefit and no NSIs; 48 (6.0%) reported neither; and 1 reported a NSI and no benefit. Differences by site (n = 5) were statistically significant ($p < 0.001$) with benefits reported by 89.1 to 98.1% of ppts. The percentage of ppts reporting a benefit decreased slightly by age in years (yrs) at enrollment (18-20yrs 229/238 = 96.2%, 21-25yrs 312/334 = 93.4%, 26-30yrs 136/146 = 93.2% and 31-35yrs 75/83 = 90.4%) but the difference was not statistically significant ($p = 0.23$). Similarly high percentages of both treatment groups, and both sexes reported a benefit at one or more study visits (vaccine 374/400 = 93.5% vs. placebo 378/401 = 94.3%; women 339/360 = 94.2% vs. men 413/441 = 93.5%). Frequently reported benefits were receiving free HIV risk reduction counselling and testing, and knowing one's HIV status. Twenty male ppts identified information about medical male circumcision was beneficial. Ppts also reported pride in doing ''something good for [their] community'', ''helping my nation'', and educating others about HIV/AIDS.
Conclusions: The majority of ppts, including those reporting negative SI events, reported benefits of study participation on their lives. Differences by site were statistically significant ($p < 0.001$). Additional examination of reported benefits of study participation may be informative, and potentially enhance future recruitment and retention efforts.

P42.02
Impact of DSMB Outcomes on Participation in HIV Prevention Trials: The VOICE Study Experience in Kampala, Uganda

Juliane Etima[1], Teopista Nakyanzi[1], Samuel Kabwigu[1], Flavia M. Kiweewa[1], Brenda G. Mirembe[1], Carolyne A. Akello[1], Lisa Rossi[2], Clemensia Nakabiito[1]

[1]MU-JHU Research Collaboration, Kampala, Uganda, [2]Microbicide Trials Network, Pittsburgh, PA, United States

Background: Clinical trials are monitored and regulated by independent bodies to ensure participants' safety and ethical conduct. Depending on study progress, these bodies may recommend a trial to continue as is, be modified or stopped. Six such reviews were conducted during the implementation of the VOICE study. We describe the impact of Data & Safety Monitoring Board (DSMB) recommendations on continued study participation in Kampala, Uganda, including retention, researchers' motivation to continue the study, and community perceptions and attitudes about the study.
Methods: Communication plans were used to disseminate DSMB outcomes to 6 tiers of stakeholders including study staff, participants, Institutional Review Board, Community Advisory Board, media, and other key stakeholders, including civil society. A qualitative analysis of DSMB outcome reports and review of participant retention was done. Discussion about different scenarios was done in advance with stakeholders.
Results: Stakeholders across the 6 tiers expressed disappointment with DSMB outcomes in VOICE. ''We are ashamed because the doctors treated many infections and we benefited. The tests were expensive and the blood samples showed we did not use the products'' (participant). ''All our effort has gone to waste'' (staff). ''HIV drugs disappoint researchers'' (media). ''We told you that your things will not work, you want to experiment on us'' (community member). The number of missed visits increased after dissemination of the Nov 2011 DSMB outcome when a second study arm (tenofovir gel) was stopped; 24% (41/171) as compared to 11% (18/171) in Sept 2011 when the first arm (tenofovir tablet) was stopped ($p < 0.001$).
Conclusions: Communication about negative DSMB outcomes remains a challenge, although communication plans make dissemination more manageable for sites. Data from VOICE suggest that DSMB outcomes may have had a significant impact on visit retention in Kampala.