

**STUDY EXAMPLE: SUCCESSFUL MENTORED ABSTRACT
FOR IAS 2009 CONFERENCE**

"The mentoring system was extremely useful and helped me convey the essential information in the abstract."

Barnabas Ruanne, South Africa

DRAFT ABSTRACT SUBMITTED FOR MENTORING

TRACK **C2**
Category C14 Efficacy trials – ancillary studies

Title:

HSV-2 is associated with HIV acquisition among both placebo and vaccine recipients in the STEP trial of the Merck Adenovirus 5 (MRKAd5) HIV-1 vaccine

Background:

The randomized clinical trial of the MRKAd5 HIV-1 vaccine (STEP study) demonstrated that the vaccine did not prevent HIV infection or reduce early viral load (VL). Moreover, increased HIV incidence was seen in vaccine recipient subgroups. HSV-2 infection is associated with increased risk of HIV acquisition and increased HIV VL. In the STEP study we examined whether volunteers with HSV-2 antibodies at baseline had increased (1) HIV acquisition, (2) VL and/or (3) faster time to antiretroviral therapy (ART) initiation.

Methods:

HSV-2 associations were explored using the primary analysis data set of 1836 men, including 88 men who were infected with HIV prior to unblinding, from North and South America, the Caribbean and Australia. HSV-2 serostatus was determined by Western blot (WB) and HIV was diagnosed by immunoassay with WB confirmation. Cox proportional hazards regression was used to estimate the association between baseline HSV-2 seropositivity and HIV acquisition and time to ART initiation among HIV seropositives. The association between HSV-2 seropositivity and early pre-ART VL was assessed using linear regression.

Results:

HSV-2 increased risk of HIV acquisition among placebo recipients; (unadjusted) uHR=2.2 (95% CI: 1.1-4.2); (adjusted) aHR=3.5 (95% CI: 1.7-7.1), controlling for male circumcision (MC), region, age, Ad5 serum antibody titer (<18, >18) and risk behavior. Among placebo and vaccine recipients we noted uHR=HR=1.7 (95% CI; 1.1-2.7); aHR=2.3 (95% CI; 1.5-3.7) controlling for vaccine, MC, region, age, Ad5 titer, risk behavior and (the significant) vaccine-circumcision interaction. No significant vaccine-HSV-2 interaction was found. No difference in pre-ART VL or time to ART initiation by HSV-2 serostatus was observed.

Conclusion:

HSV-2 increased the risk of HIV association in both placebo and vaccine recipients in the STEP trial by 2-3 fold. Adjusting for HSV-2 did not change the increased risk of HIV-1 acquisition associated with the vaccine found in the primary analysis.

FEEDBACK FROM MENTOR

Track and Title

1. Is the track chosen appropriate?

Response: Selected track is appropriate

2. Does the title reflect the content of the abstract?

Response: The title reflects the contents of the abstract suitably

Structure

1. Does the abstract follow scientific and formal criteria?

Response: The abstract follows the conference abstract guidelines, and also follows generally accepted scientific and formal criteria - there is a clear study objective, an intervention, results, and a brief analysis of results.

2. Do the ideas cohere together?

Response: The ideas are cogent, and cohere strongly

3. Does each section provide relevant information?

Response: Yes.

Language/Grammar

1. Is correct terminology used?

Response: Yes.

2. Is the spelling correct?

Response: Yes. Only one probable spelling error (in the results section, first sentence.....Ad5 serum antibody titer (<18, >18))

3. Is the language concise and clear?

Response: Yes

4. Is the abstract well-written and easy to follow?

Response: Yes, The abstract is easy to follow

SCIENTIFIC DESIGN:

Background

1. Are the objectives clear and well-presented?

Response: Yes .

2. Is the research design sound?

Response: The research design is very strong

Materials/methods

1. Is the methodology used appropriate for the study?

Response: Yes

2. Is it easy to understand what methods the author(s)s have used and why?

Response: Yes. However, the methods section would be further strengthened if it cited the number of individuals with a positive HSV-2 WB result at baseline. It might also be helpful (depending on word limit) to cite the number of individuals from the entire cohort who initiated ART prior to the end of the study, as this is one of the clinical end points

3. Is the data analysis and interpretation appropriate?

Response: Yes. However, a generic variable called risk behavior is included in the Cox proportional hazards regression. What does this consist of? Depending on the word limit, a suggestion for the author(s) is to include a brief note on loss to follow up or drop-out from the study, as this could be a factor confounding the time to ART initiation variable.

Results/Conclusions

1. Are the conclusions clearly explained and appropriate to the study?

Response: Yes.

2. Is the study innovative? Does it provide new insights?

Response: The study further strengthens the body of evidence on HIV prevention.

3. Are the results analyzed in a broader context?

Response: There is no discussion of the broader policy, practice, or standards implications of the results of the study. This may or may not have been a conscious decision on the part of the author(s)

4. Are the future implications of this study discussed?

Response: No. This may or may not have been a conscious decision on the part of the author(s).

Title: Herpes simplex type 2 (HSV-2) is associated with HIV acquisition among both placebo and vaccine recipients in the STEP trial of the Merck Adenovirus 5 (MRKAd5) HIV-1 vaccine

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Background: The randomized clinical trial of the MRKAd5 HIV-1 vaccine (Step study) demonstrated that the vaccine did not prevent HIV infection or reduce early viral load (VL). Moreover, in some subgroups, HIV incidence was higher in vaccinees than in placebo recipients. HSV-2 infection is associated with increased risk of HIV acquisition and elevated HIV VL. We examined whether trial volunteers with HSV-2 antibodies at baseline had (1) increased HIV acquisition, (2) elevated VL and/or (3) faster time to ART initiation.

Methods: HSV-2 associations were explored using the primary analysis data-set of 1836 men from North and South America, the Caribbean and Australia, including 88 men infected with HIV prior to unblinding. HSV-2 serostatus was determined by Western blot (WB) and HIV was diagnosed by immunoassay with WB confirmation. Cox proportional hazards regression models were used to estimate the association between HSV-2 seropositivity and HIV acquisition and time to ART initiation among HIV seropositives. The association between HSV-2 seropositivity and early pre-ART VL was assessed using linear regression.

Results: Baseline HSV-2 seroprevalence was 30% (n=550). HSV-2 increased risk of HIV-1 acquisition among placebo recipients; (unadjusted) uHR=2.2 [95%CI: 1.1-4.2]; (adjusted) aHR=3.5 [1.7-7.1], controlling for male circumcision (MC), region, age, baseline Ad5 serum antibody titer ($\leq 18, >18$) and risk behavior. Among all participants we noted uHR=1.7 [1.1-2.7]; aHR=2.3 [1.5-3.7] controlling for vaccine, MC, region, age, Ad5, risk behavior and vaccine-circumcision interaction. Controlling for HSV-2 did not change the vaccine effect among uncircumcised men (aHR=3.27 [1.39-7.68] compared with HR=2.65 [1.18-5.97]). No significant vaccine-HSV-2 interaction was found. No difference in pre-ART VL or time to ART initiation by HSV-2 serostatus was observed.

Conclusions: Baseline HSV-2 seropositivity was associated with a 2-3 fold increased risk of HIV acquisition. Adjusting for HSV-2 did not account for the higher HIV-1 acquisition rate observed in the vaccine group in the primary analysis.

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Abstract no. TUAC201

Suggested Citation

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