Immunogenicity and Reactogenicity of Cervarix® Versus Gardasil® in HIV-Infected Adults: An RCT

Lars Toft[1], Merete Storgaard[1], Martin Müller[2], Peter Sehr[3], Jesper Bonde[4,5], Martin Tolstrup[1], Lars Østergaard[1] and Ole S. Søgaard[1]

1) Department of Infectious Diseases, Aarhus University Hospital, 8200 Aarhus, Denmark
2) Research Program Infection and Cancer, German Cancer Research Center, Im Neuenheimer Feld 242, 69120 Heidelberg, Germany
3) Chemical Biology Core Facility, European Molecular Biology Laboratory, Meyerhofstraße 1, 69117 Heidelberg, Germany
4) Department of Pathology, Copenhagen University Hospital Hvidovre, Denmark
5) Clinical Research Centre, Copenhagen University Hospital Hvidovre, Denmark

Contact: Ole Schmeltz Søgaard, Department of Infectious Diseases, Aarhus University Hospital, Skejby, 8200 Aarhus, Denmark.
Fax: +4578452848, Telephone number: +4578452842 Email: olesoega@rm.dk.

ABSTRACT

Objectives: To compare the immunogenicity and reactogenicity of Cervarix® or Gardasil® Human Papillomavirus (HPV) vaccines in HIV-infected adults.

Methods: A double-blind, controlled trial randomizing HIV-positive adults to receive three doses of Cervarix® or Gardasil® at 0, 1.5 and 6 months. Immunogenicity was evaluated for up to 12 months. Neutralizing anti-HPV-16/18 antibodies were measured by pseudovirion-based neutralization assay (PBNA). Laboratory tests and diary cards were used for safety assessment. The HPV-DNA status of the participants was determined before and after immunization.

Results: Ninety-two participants were included in the study. Anti-HPV-18 antibody titers were higher in the Cervarix® group compared with the Gardasil® group at 7 and 12 months. No significant differences in anti-HPV-16 antibody titers were found among vaccine groups. Among Cervarix® vaccinees, women had higher anti-HPV-16/-18 antibody titers compared to men. No gender-specific differences in antibody titers were found in the Gardasil® group. Mild injection site reactions were more common in the Cervarix® group than in the Gardasil® group (91.1% vs. 69.6%; P = .02). No serious adverse events occurred.

Conclusions: Both vaccines were immunogenic and well tolerated. Compared with Gardasil®, Cervarix® induced superior vaccine responses among HIV-infected women whereas in HIV-infected men the difference in immunogenicity was less pronounced.

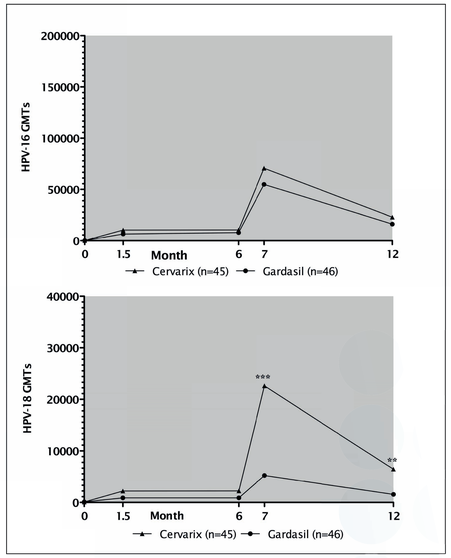


Figure 1: HPV serotype-specific neutralizing antibody geometric mean titers (GMTs).
HPV serotype-specific neutralizing antibody geometric mean titers (GMTs) computed using the log10 transformation of ED50 values for anti-HPV-16 and HPV-serum neutralizing antibodies as measured by pseudovirion neutralization assay at months 0, 1.5, 6, 7, and 12. ** P < .001, *** P<.0001. One study participant from the Cervarix group withdrew after second visit and one study participant from the Gardasil group was lost to follow up after fourth visit.

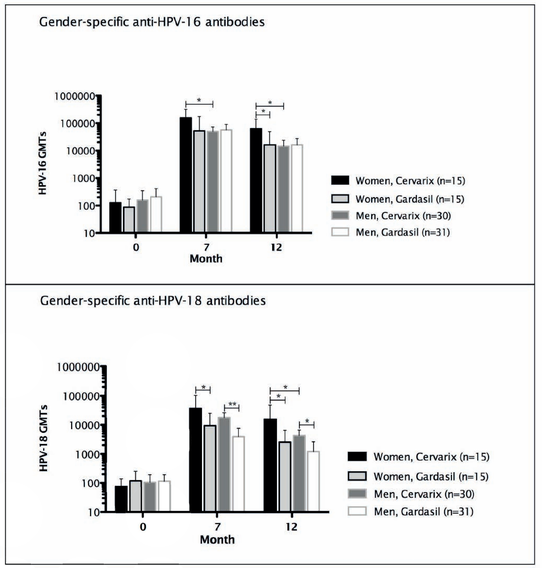


Figure 2: HPV serotype-specific neutralizing antibody geometric mean titers (GMTs) stratified according to gender.
GMTs computed using the log10 transformation of ED50 values for anti-HPV-16 and anti-HPV-18 serum neutralizing antibodies measured by pseudovirion neutralization assay at months 0, 7 and 12. * P < .05; ** P < .001.
One woman from the Cervarix group withdrew before the month 7 and one man from the Gardasil group was lost to follow up before month 12.

METHODS

Study Design: This was an investigator-initiated, randomized, double-blind head-to-head trial randomizing persons with HIV to vaccination with either Cervarix® or Gardasil®. The study was conducted at the Department of Infectious Diseases, Aarhus University Hospital, Denmark. Participants were stratified according to use of HAART and gender and thereafter randomized 1:1 in blocks of 4 to receive Cervarix® or Gardasil®. Participants received vaccination with either Cervarix® or Gardasil® at month 0, 1.5 and 6 and they were seen at month 7 and 12 for immunogenicity and safety follow up.

RESULTS

Immunogenicity: Primary endpoints are shown in Figure 1. Both vaccines increased HPV-16 GMTs from baseline to 7 and 12 months and no significant differences in anti-HPV-16 antibody titers were found between vaccine groups. Anti-HPV-18 GMTs were higher in the Cervarix® group Compared with the Gardasil® group at 7 and 12 months. The GMT ratio was 4.31 at 7 months (95% confidence interval [CI]: 2.21–8.40) and 4.15 at 12 months (95% CI: 1.95–8.84).

Safety: No serious adverse events were detected in this study. Both vaccines were generally well-tolerated and very few mild systemic reactions were observed. Injection site reactions were more common in the Cervarix® compared with the Gardasil group® (91.1% vs 69.6%; P = .02).

SUMMARY

In the present study we found that Cervarix® was significantly more immunogenic than Gardasil® in HIV-infected women. However, this difference in immunogenicity was less pronounced in HIV-infected men where the two vaccines induced similar antibody responses against HPV-16 but higher anti-HPV-18 antibodies for Cervarix® than Gardasil®. Mild injection site reactions were more common in the Cervarix® group. Collectively, our findings suggest that Cervarix® is superior to Gardasil® in terms of inducing protective immunity against oncogenic HPV-16 and HPV-18 infection in HIV-infected women. However, whether this difference translates into enhanced or prolonged protection against cervical cancer is still unknown.

Layout: Kommunikation Aarhus Universitetshospital - 05021145