

LATEST PAPERS

SEARCH for PAPERS

Printer-friendly PDF

Comment(s)

[>Abstract](#) [>References](#)

Cancer Immunity, Vol. 3 Suppl. 1, p. 25 (6 February 2003)

Immunotherapy for HPV associated pre-cancer

Ian H. Frazer^{1*}, G.J. Leggatt¹, K. Matsumoto¹, R. De Klyver¹, M. Quinn², J. Nicklin³, J. Tan², L. Perrin³, P. Ng⁴, V. O'Connor⁵, O. White¹, N. Wendt¹, J. Martin¹, S.V. Mitchell⁶, A. McKenzie⁶, J. Crowley⁶, S. Edwards⁶, and D. Maher⁶

¹Centre for Immunology and Cancer Research, The University of Queensland, Princess Alexandra Hospital, Brisbane, Queensland

²Royal Women's Hospital, Parkville, Victoria

³Royal Women's Hospital, Brisbane, Queensland

⁴Mater Mother's Hospital, Brisbane, Queensland

⁵Queen Elizabeth II Jubilee Hospital, Brisbane, Queensland

⁶CSL Limited, Parkville, Victoria, Australia

*Presenting author

Abstract

Cervical pre-cancer is associated with, and develops from, infection of cervical epithelium by one of a range of oncogenic papillomaviruses. To model the immunology of papillomavirus infection, we have grafted skin transgenic for the E7 major transforming protein of HPV16 to naive recipient mice (1). We examined the nature of the immune response to E7 developed following grafting, the effect of E7 specific-immunotherapy on graft outcome, and the nature of the immune response, which can result in graft destruction. Grafting to transgenic skin in which E7 or hGH is expressed in epithelial cells from a keratin 14 promoter to a naive animal induces active tolerance of the graft antigen, and this tolerance is not broken by immunization. Co-administration of a strong pro-inflammatory signal at the time of grafting E7 transgenic skin results in graft rejection, and animals that have rejected one E7 graft will specifically reject a further E7 transgenic graft without further immune manipulation. Graft rejection requires both CD4 and CD8 T cells, and antigen specific rejection response can be determined either by CD4 cells or by CD8 cells.

To establish the safety, tolerability and immunogenicity of HPV16 specific immunotherapy for CIN in patients with CIN, we conducted a double blind trial using CerVax16™, a fusion protein of E6 and E7 from HPV16 combined with ISCOMs, a saponin based adjuvant. 31 women with CIN 1-3 were randomly allocated to receive active treatment (n = 24) with one of three dose levels of antigen (20 µg, 60 µg, or 200 µg), or placebo (n = 7). Up to three injections were given intramuscularly over 6 weeks. Subjects were assessed for adverse events, immunogenicity, and HPV16 viral load in cervical biopsies taken before and after treatment. Local site reaction (mild n = 11, moderate n = 11, severe n = 2) and systemic symptoms (mild n = 11, moderate n = 8, severe n = 3) were observed in active and placebo groups. Specific antibody was induced for all 24 subjects given active vaccine. 12 of 20 evaluable subjects given active vaccine demonstrated a gamma-interferon response. CTL responses were detected in some subjects. In general, responses increased with multiple vaccinations. No major changes in colposcopic appearance or in cervical histology were observed. Of 14 HPV16 +ve subjects treated, 13 had lower mean HPV copy number per cell after treatment. Mean viral load fell from 50 ± 22 viral copies per cell pre-treatment to 12 ± 8 post-treatment ($P < 0.05$; paired *t* test). Mean viral load did not fall significantly in women given placebo ($P = 0.34$). CerVax16™ is thus safe and immunogenic in patients with HPV16-associated CIN, and may reduce the load of HPV16 in infected cervical tissue.

References

1. Frazer IH, De Kluyver R, Leggatt GR, Guo HY, Dunn L, White O, Harris C, Liem A, Lambert P. Tolerance or immunity to a tumor antigen expressed in somatic cells can be determined by systemic proinflammatory signals at the time of first antigen exposure. *J Immunol* 2001; **167**: 6180-7. (PMID: 11714778)

Copyright © 2003 by Ian H. Frazer