

HspE7 Treatment of Anal Dysplasia: Results of an Open Label Trial of HspE7 and Comparison with a Prior Controlled Trial of Low Dose HspE7

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Background: Human papillomavirus (HPV) causes anogenital squamous intraepithelial lesions (SIL) and anogenital cancer. Since treatment of anal SIL often requires surgery, we tested a novel HPV-specific immunotherapy.

Methods: We made HspE7, fusing heat shock protein Hsp65 from BCG to E7 protein from HPV16. Patients (pts) with anal high grade (H) SIL entered a randomized, placebo controlled trial of HspE7, 100 mcg monthly x3 (study "9901"). One month (m) after the completion of treatment, pts with persistent SIL were eligible to cross to an open label trial of HspE7, 500 mcg monthly x3 (study "9902"). Response was taken as the most severe diagnosis after high resolution anoscopy with cytology and biopsy. HPV was typed by PCR analysis of anal swab. We report 6 m results from the first 56 consecutive pts in 9902 and final data from 9901. **Results:** In 9901, the overall response was 17/85 (20%) and there was no difference between active treatment (21%) and placebo (19%). At 6 m in 9902, 40/56 (71%) pts downgraded to anal low grade (L) SIL. The response rate in the open label trial was not dependent on the treatment received in the randomized trial. 76/82 subjects in 9902 reported adverse experiences (AE) related to HspE7: most commonly, injection site reactions and asthenia, but no severe or serious AE. More AE were seen with high dose HspE7 than with low dose. 7/52 pts and 3/37 responders were HPV16+. **Conclusions:** Pathological data suggest that HspE7 (500 mcg x3) is active in treatment of anal HSIL, converting most pts from HSIL to LSIL. High dose is superior to low dose and low dose is not superior to placebo. Response appears not to be HPV16-specific. HspE7 500 mcg monthly x 3 is well tolerated in this population. A double-blind placebo-controlled of the 500 mcg regimen is currently in progress.