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Efficacy of Heat Shock Protein-Based Therapy for Carcinoma-In-Situ of the Cervix

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Abstract:

Objectives: SGN-00101 (HspE7, Nventa, San Diego, CA) is a novel fusion protein therapeutic vaccine consisting of an *M. Bovis* BCG heat shock protein (Hsp65) covalently linked to the entire sequence of HPV 16 E7. This is an extended analysis of the original (cohort 1) and extended observation groups (cohort 2) of an NCI-sponsored Phase II trial (NCI 5850) designed to evaluate the efficacy and toxicities of HspE7 in women with CIN III.

Methods: HIV (-) women with biopsy-proven CIN III were eligible. The cohort 1 sample size assumed a single stage Phase II design and a 4 month regression rate of 10% in an untreated population and a target response rate of 35%. After established safety and efficacy in cohort 1, a second cohort of 26 patients was accrued for added precision. Each patient underwent 3 monthly subcutaneous vaccinations with 500 µg of HspE7 followed by monthly colposcopic follow-up for 1 month in cohort 1 and 3 months in cohort 2. All patients then underwent a LEEP. A complete pathologic response (pCR) was defined as no evidence of CIN or CIN I (HPV changes only). A partial response (PR) was defined as colposcopic regression of the lesion by >50%. Cervicovaginal lavage samples were obtained at each visit for HPV typing using MY09/ MY11 HPV PCR.

Results:

71 patients were registered, of whom 63 were eligible after screening. 57 patients completed the trial and were evaluable (31 in cohort 1, 26 in cohort 2). There were no significant epidemiologic or HPV type differences between the 2 cohorts so responses were combined for analysis. Of the 57 patients, 12 (21%) had a pCR; 32 (56%) had a PR and 11 (19%) had stable disease. 2 (4%) patients in cohort 2 progressed (microinvasive) during the trial. The overall response rate was 44/57 (77%, 95% C.I.=66-88%). 29/57 (51%) were HPV 16 positive prior to vaccination and 3 patients had HPV 16 subsequently detected. Regression was likely in patients without HPV 16 compared to those with HPV 16 (86% vs. 66%; p=0.05). Similar responses were seen in patients infected with multiple HPV types compared with those infected with 1 type (p=0.20).

Conclusions:

HspE7 appeared efficacious for treatment of women with CIN III and met a priori assumptions for efficacy; however, it is unclear at present whether this was due to natural regression alone. HspE7, which targets the HPV 16 E7 oncoprotein, had efficacy in

patients infected with HPV types other than 16, suggesting cross-reactivity. A larger randomized, controlled trial is needed to better define efficacy and to identify subsets of women most likely to benefit from immunotherapy.

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