

Identification of antibody responses induced in patients with biochemically recurrent and castration-resistant prostate cancer receiving GVAX immunotherapy for prostate cancer

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Abstract

Background: GVAX immunotherapy for prostate cancer is comprised of 2 allogeneic prostate carcinoma cell lines (PC-3 and LNCaP) that have been modified to secrete GM-CSF. Studies completed to date include G-9802, a multicenter phase 1/2 trial in patients (pts) with biochemical (PSA) recurrence following prostatectomy or radiation therapy, and G-0010, a multicenter phase 2 trial in pts with CRPC.

Methods: Immunotherapy-induced antibody (Ab) responses were evaluated in 14 pts from G-0010 whose actual survival exceeded that predicted by the Halabi nomogram using 2 methods: i) serological analysis of gene expression (SEREX) and ii) protein chip analysis. Ab responses observed in at least 2 of these 14 pts were then further examined in all evaluable G-0010 ($n = 65$) and G-9802 ($n = 19$) pts. Ab responses were evaluated for potential association with survival using the Cox regression model (G-0010) and for effect on PSA slope and doubling-time (PSADT) using Wilcoxon rank sum test (G-9802).

Results: Analysis of Ab responses in 14 CRPC pts yielded 411 candidate Ags, of which 93 were seen in 2 or more pts. Preliminary data from evaluable G-0010 pts suggest that Abs to protein FLJ14668, neuronatin, cardiolipin and HLA-A24 may be associated with survival independently of treatment duration and prognostic factors. Exploratory analyses in evaluable G-9802 pts showed a positive association between induction of Ab to filamin-B (FLNB) and post-treatment declines in PSA slope ($P = 0.0226$). PSADT increased by a median of 85 weeks in patients with an anti-FLNB response ($n = 6$) vs. 10 weeks in those without ($n = 13$; $P = 0.011$).

Conclusions: GVAX immunotherapy for prostate cancer induces a polyvalent IgG Ab response. The majority of proteins targeted are patient-specific; however, a smaller group of higher frequency Ab targets were identified. Apparent associations of Abs to multiple proteins with survival and PSA kinetics were observed in G-0010 and G-9802, respectively, and will be evaluated prospectively in ongoing phase 3 trials of GVAX immunotherapy for prostate cancer with the goal of identifying potential biomarkers of response.