Interim Analysis of Phenelzine (a Monoamine Oxidase Inhibitor) for Non-metastatic Recurrent Prostate Cancer

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Background: Monoamine oxidase A (MAOA) is an androgen regulated gene [1] which is highly expressed in high grade prostate cancer [2] and effects prostate tumor formation and metastasis [3]. Thus, we initiated a clinical trial to explore anti-cancer effects of phenelzine (Nardil, an irreversible MAOA/B inhibitor) in patients with recurrent prostate cancer.

Methods: Eligibility included patients with elevated PSA after primary therapy defined by: PSA ≥ 0.4 ng/ml (post-prostatectomy) or PSA ≥ 2 ng/ml above a post-therapy nadir (post-radiation therapy or primary androgen deprivation therapy) and no evidence of metastatic cancer on imaging studies. Patients are enrolled into cohorts with an open-label design based on testosterone levels to receive a target dose of phenelzine 30 mg orally twice daily.

The primary endpoint is the proportion of patients who achieve a PSA decline of ≥50% from baseline. A preliminary analysis was performed after 12 evaluable patients were enrolled according to the a Simon minimax two-stage design to define the probability of response to phenelzine (P1) as ≥20% and reject the drug if the response probability (P0) is ≤ 5% with power set at 0.8 [3].

Results: Twelve patients have been enrolled in the non-castrate group. 2 subjects have demonstrated ≥50% maximum decline in PSA level. Maximal PSA declines varying between 1-44% have been observed in 5 other subjects in the non-castrate group. The profile of adverse events (AE) varied greatly across subjects. Common toxicities observed included fatigue, dizziness, edema, and hypertension which were generally grade 1.

Conclusion: The preliminary finding of ≥50% PSA decrease in 2/12 = 17% meets pre-specified criteria for continued enrollment towards the goal of 21 evaluable subjects in the non-castrate group. "Partial" PSA declines were observed in 5/12 = 42% of subjects. Enrollment of subjects with both non-castrate and castrate levels of circulating androgens continues. ClinicalTrials.gov Identifier: NCT02217709

Conflicts of Interest: Patent pending to Jean C. Shih, Ph.D.

Funding: USC- Taiwan Center for Translational Research supported by Tsai Family Fund to Jean C. Shih.

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