Gene expression profiles associated with stable disease in metastatic castration-resistant prostate cancer patients treated with ADXS-PSA immunotherapy

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INTRODUCTION

Active immunotherapy, such as ADXS-PSA, is designed to elicit an antitumor response by targeting the immune system.

ADXS-PSA is a highly attenuated (vaccine dosing) (A) based immunotherapy that targets prostate-specific antigen (PSA), a secretory protein involved in a treatment for previously metastatic castration-resistant prostate cancer (mCRPC). In the phase 1/2 ADXS-PSA trial (clinicaltrials.gov NCT00965503, Phase 1, open label), patients were treated with ADXS-PSA (vaccines) by subcutaneous injection (oral, non-vaccines) in combination withKEYTRUDA (pembrolizumab) (Part II, enrolling).

Advance’s·based immunotherapies act by redirecting innate immunity through multiple mechanisms including the STING pathway, by reducing the numbers and activity of immune-suppressors cells, in the hope of reducing the levels of antigen-specific T cells that infiltrate and destroy the tumor.

Because of their ability to modify immune responses (Part II), advances tailored to patient’s specific immune status (Part II), such as chemotherapy and radiation therapy, may have an impact on the clinical outcome of patients with metastatic prostate cancer (mCRPC).

For this reason, we examined the innate status of previously treated mCRPC patients, particularly in the context of stable disease, and hypothesized that immune status may be associated with clinical outcomes.

OBJECTIVES

- Assess innate status of ADXS-PSA patients who have been previously treated with standard of care therapy, and evaluate the change in the gene expression levels in PBMCs from their PBMCs before and after ADXS-PSA treatment.

- Determine which gene expression profiles were associated with clinical response to ADXS-PSA monotherapy.

MATERIALS AND METHODS

The ADXS-PSA trial (NCT01633557) is a phase 1/2 evaluation of ADXS-PSA alone (Part I) and in combination with KEYTRUDA (pembrolizumab) (Part II) in metastatic prostate cancer (mCRPC). The study design for the ADXS-PSA trial is summarized in Figure 1.

- Immunogen-related gene expression levels in PBMCs isolated at 3 time points during the first 9 weeks of treatment from 40 ADXS-PSA patients participating in the Part I ADXS-PSA dose-escalation trial (NCT01633557) were analyzed.

- Nanotechnology Platform Immune Profiling data was used to quantify gene expression levels.

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- Differential expression analysis was conducted on normalized Nanotechnology Platform Immune Profiling gene data for 32 patients, including 29 patients treated with ADXS-PSA alone and 3 other ADXS-PSA treatments.

RESULTS

- Immunogen-related gene expression levels were assessed in PBMCs isolated at 3 time points during the first 9 weeks of treatment from ADXS-PSA patients participating in the Part I ADXS-PSA dose-escalation trial (NCT01633557) were analyzed.

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- Table 1 summarizes the baseline demographics of the patients who did and did not achieve stable disease.

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- Table 2 summarizes the differential gene expression analysis, which was performed using the R statistical software.

- The results of the differential gene expression analysis are shown in Table 2.

CONCLUSIONS

- Additional immunotherapies are needed to elicit an antitumor response by targeting the immune system.

- In patients with previously treated metastatic prostate cancer, ADXS-PSA treatment may have a significant impact on the clinical outcome of patients with metastatic prostate cancer (mCRPC).

- The results of the differential gene expression analysis are shown in Table 2.

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REFERENCES