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Prospective assessment of a gene signature potentially predictive of clinical benefit in metastatic melanoma patients following MAGE-A3 immunotherapeutic (PREDICT)

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Background: Genomic profiling of tumor tissue may aid in identifying predictive or prognostic gene signatures (GS) in some cancers. Retrospective gene expression profiling of melanoma and non-small-cell lung cancer led to the characterization of a GS associated with clinical benefit, including improved overall survival (OS), following immunization with the MAGE-A3 immunotherapeutic. The goal of the present study was to prospectively evaluate the predictive value of the previously characterized GS.

Patients and methods: An open-label prospective phase II trial ('PREDICT') in patients with MAGE-A3-positive unresectable stage IIIB-C/IV-M1a melanoma.

Results: Of 123 subjects who received the MAGE-A3 immunotherapeutic, 71 (58.7%) displayed the predictive GS (GS+). The 1-year OS rate was 83.1%/83.3% in the GS+/GS– populations. The rate of progression-free survival at 12 months was 5.8%/4.1% in GS+/GS– patients. The median time-to-treatment failure was 2.7/2.4 months (GS+/GS–). There was one complete response (GS–) and two partial responses (GS+). The MAGE-A3 immunotherapeutic was similarly immunogenic in both populations and had a clinically acceptable safety profile.

Conclusion: Treatment of patients with MAGE-A3-positive unresectable stage IIIB-C/IV-M1a melanoma with the MAGE-A3 immunotherapeutic demonstrated an overall 1-year OS rate of 83.5%. GS– and GS+ patients had similar 1-year OS rates, indicating that in this study, GS was not predictive of outcome. Unexpectedly, the objective response rate was lower in this study than in other studies carried out in the same setting with the MAGE-A3 immunotherapeutic. Investigation of a GS to predict clinical benefit to adjuvant MAGE-A3 immunotherapeutic treatment is ongoing in another melanoma study.This study is registered at www.clinicatrials.gov NCT00942162.

Key words: MAGE-A3 antigen, gene signature, melanoma, immunotherapy, predictive biomarkers

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