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


1General Dermatology and Oncology Service, Ambroise-Paré Hospital, AP-HP, University of Versailles-Saint-Quentin-en-Yvelines, Boulogne, France; 2Skin Cancer Center Hannover, Hannover Medical School, Hannover, Germany; 3National Institute for Tumors Foundation ‘G. Pascale’, Naples; 4Medical Oncology and Immunotherapy, Department of Oncology, University Hospital of Siena, Istituto Toscano Tumori, Siena, Italy; 5Department of Dermatology and Skin Cancers, La Timone APHM Hospital, Aix-Marseille University, Marseille, France; 6Department of Biochemistry and Molecular Biology, Poznań University of Medical Sciences, Poznań, Poland; 7Dermatology Clinic, Hôtel-Dieu Hospital, CHU Nantes, Nantes, France; 8Department of Surgical Oncology, UTMD Anderson Cancer Center, Houston; 9Moffitt Cancer Center, Tampa, USA; 10Department of Dermatology, University Hospital Schleswig-Holstein, Kiel, Germany; 11Department of Soft Tissue/Bone Sarcoma and Melanoma, Maria Sklodowska-Curie Memorial Center and Institute of Oncology, Warsaw, Poland; 12Melanoma and Soft Tissue Sarcoma Division, European Institute of Oncology, Milan, Italy; 13Petrov Research Institute of Oncology, St. Petersburg, Russian Federation; 14Department of Dermatology, University of Heidelberg, Heidelberg, Germany; 15Department of Dermatology, University Hospital of Breis, Brest, France; 16GSK Vaccines, Rixensart, Belgium

Received 10 January 2016; revised 26 May 2016; accepted 20 July 2016

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.clinicaltrials.gov NCT00942162.

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

*Correspondence to: Prof. Philippe Saiag, Service de Dermatologie Générale et Oncologique, Hôpital Ambroise-Paré, Assistance Publique-Hôpitaux de Paris, Université Versailles-Saint-Quentin-en-Yvelines, 9 av Charles de Gaulle Boulogne-Billancourt 92104 Boulogne, France. Tel: +33-1-49-09-56-73; Fac: +33-1-49-09-56-85; E-mail: philippe.saiag@uvsq.fr

†Present address: NuCana BioMed Ltd, Edinburgh, UK.
‡Present address: Vanova Biosciences, Belgium.
§Present address: Servier, Suresnes, France.

© The Author 2016. Published by Oxford University Press on behalf of the European Society for Medical Oncology. This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/4.0/), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact journals.permissions@oup.com