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

P. Saiag, R. Gutzmer, P. A. Ascierto, M. Maio, J.-J. Grob, P. Murawa, Brigitte Dréno, M. Ross, J. Weber, A. Hauschild, et al.

*Annals of Oncology* 27: 1947–1953, 2016
doi:10.1093/annonc/mdw291
Published online 8 August 2016

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

P. Saiag[1*], R. Gutzmer[2], P. A. Ascierto[3], M. Maio[4], J.-J. Grob[5], P. Murawa[6], B. Dreno[7], M. Ross[8], J. Weber[9], A. Hauschild[10], P. Rutkowski[11], A. Testori[12], E. Levchenko[13], A. Enk[14], L. Misery[15], C. Vanden Abeele[16], I. Vojtek[16], O. Peeters[16,†], V. G. Brichard[16,‡] & P. Therasse[16,§]

*[1]General Dermatology and Oncology Service, Ambroise-Paré Hospital, AP-HP, University of Versailles-Saint-Quentin-en-Yvelines, Boulogne, France; [2]Skin Cancer Center Hannover, Hannover Medical School, Hannover, Germany; [3]National Institute for Tumors Foundation 'G. Pascale', Napoli; [4]Medical Oncology and Immunotherapy, Department of Oncology, University Hospital of Siena, Istituto Toscano Tumori, Siena, Italy; [5]Department of Dermatology and Skin Cancers, La Timone APHM Hospital, Aix-Marseille University, Marseille, France; [6]Department of Biochemistry and Molecular Biology, Poznań University of Medical Sciences, Poznań, Poland; [7]Dermatology Clinic, Hôtel-Dieu Hospital, CHU Nantes, Nantes, France; [8]Department of Surgical Oncology, UTMD Anderson Cancer Center, Houston; [9]Moffitt Cancer Center, Tampa, USA; [10]Department of Dermatology, University Hospital Schleswig-Holstein, Kiel, Germany; [11]Department of Soft Tissue/Bone Sarcoma and Melanoma, Maria Sklodowska-Curie Memorial Center and Institute of Oncology, Warsaw, Poland; [12]Melanoma and Soft Tissue Sarcoma Division, European Institute of Oncology, Milan, Italy; [13]Petrov Research Institute of Oncology, St Petersburg, Russian Federation; [14]Department of Dermatology, University of Heidelberg, Heidelberg, Germany; [15]Department of Dermatology, University Hospital of Brest, Brest, France; [16]GSK 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.clinicatrials.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; Fax: +33-1-49-09-56-85; E-mail: philippe.saiag@uvsq.fr

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