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ABBREVIATIONS

Abbreviations are defined in the text when they are used for the first time. Abbreviations that appear several times in the text, tables or figures are in the list below.

A

AA	Amino acid
AJCC	American Joint Committee on Cancer
ALVAC	Albany vaccine
AS02B	GlaxoSmithKline Biologicals adjuvant system 2B
AS15	GlaxoSmithKline Biologicals adjuvant system 15
ATP	Adenosine triphosphate
AVL	Antoni van Leeuwenhoek Hospital, The Netherlands Cancer Institute, Amsterdam, The Netherlands
AZN	Academisch Ziekenhuis Nijmegen, Nijmegen, The Netherlands
AZVU	Academisch Ziekenhuis Vrije Universiteit, Amsterdam, The Netherlands

B

BB	Institut Jules Bordet, Brussels, Belgium
BCG	Bacille Calmette-Guérin
BCNU	Bis-chloroethyl-cyclohexyl-nitrosourea (carmustine)
bFGF	Basic fibroblast growth factor
BTDG	Biological Treatments Development Group (EORTC)

C

CCND1	cyclin D1
CDDP	*Cis*-diamine-dichloro-platine (cisplatine)
CDKN2A	Gene coding for the cyclin-dependent kinase inhibitor $p16^{INK4A}$
CDK4	Cyclin-dependent kinase 4
CF	Centre Jean Perrin, Clermont-Ferrand, France
CHO	Chinese hamster ovary cells
CHUV	Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland
CNS	Central nervous system
CP	Institut Curie, Paris, France
CpG	Cytosine linked to a guanine by a phosphate bond
CpG 7909	A synthetic, single stranded oligodeoxyribonucleotide for human use
CPO	Centre Pluridisciplinaire d'Oncologie, CHUV, Lausanne, Switzerland
CR	Complete response
CTL	Cytolytic T lymphocyte
CTLA-4	Cytolytic T lymphocyte antigen-4
CTLp	Cytolytic T lymphocyte precursor
CUMG	Cliniques Universitaires UCL de Mont-Godinne, Yvoir, Belgium
CUSL	Cliniques Universitaires UCL Saint-Luc, Brussels, Belgium
CVD	Cisplatine, vinca alkaloid (vinblastine or vindesine), DTIC

D

d	Day
DC	Dendritic cells
DDHK	Erasmus Medical Center - Daniel den Hoed Cancer Center, Rotterdam, The Netherlands
DKFZ	Deutsches Krebsforschungszentrum, Mannheim, Germany
DMSO	Dimethyl sulfoxide
DNA	Deoxyribonucleic acid
DNP	Dinitrophenyl
DTIC	Dimethyl-triazeno-imidazole-carboxamide (dacarbazine)

DTH	Delayed-type hypersensitivity
E	
EB	Hôpital Erasme, ULB, Brussels, Belgium
EBV-B	Epstein-Barr virus-transformed B lymphocytes
ELISA	Enzyme-linked immunosorbent assay
ELISPOT	Enzyme-linked immunospot
EN	Centre Hospitalier Universitaire Michallon, Grenoble, France
EORTC	European Organization for Research and Treatment of Cancer
EU	ELISA units
G	
GCP	Good Clinical Practice
GD	Hospital Virgen de las Nieves, Granada, Spain
GM-CSF	Granulocyte/macrophage-colony stimulating factor
gp	Glycoprotein
GSK	GlaxoSmithKline Biologicals
H	
HA	Medizinische Hochschule Hannover, Hannover, Germany
HLA	Human leukocyte antigen
HM	Hôpital Henri Mondor, Creteil, France
HSP	Heat shock protein
HSPPC	HSP-peptide complexes
HUG	Hôpital Cantonal Universitaire de Genève, Geneva, Switzerland
I	
ICH	International Conference on Harmonization
ICRL	Imperial Cancer Research Fund, Leeds, United Kingdom
i.d.	Intradermally
IDO	Indoleamine 2,3-dioxygenase
IFA	Incomplete Freund's adjuvant
IFN	Interferon
IGR	Institut Gustave Roussy, Villejuif, France
IJB	Institut Jules Bordet, Brussels, Belgium
IL	Interleukin
ILP	Isolated limb perfusion
i.m.	Intramuscularly
IU	International units
i.v.	Intravenously
K	
KI	Karolinska Institutet Radiumhemmet, Stockholm, Sweden
KUL	Katholieke Universiteit Leuven, Leuven, Belgium
L	
LAK	Lymphokine-activated killer cell
LAU	Ludwig Institute for Cancer Research, Lausanne branch, Lausanne, Switzerland
LB	Ludwig Institute for Cancer Research, Brussels branch, Brussels, Belgium
LD	Longest diameter
LDH	Lactate dehydrogenase
LE	Leiden University Medical Center, Leiden, The Netherlands
LG	Université de Liège, Liège, Belgium
LICR	Ludwig Institute for Cancer Research

LM	Ludwig Institute for Cancer Research, Melbourne branch, Melbourne, Australia
LUD	Ludwig Institute clinical study number
LY	Centre Léon Bérard, Lyon, France

M

MA	Institut Paoli-Calmettes and Hôpital Sainte-Marguerite, Marseille, France
MAGE	Melanoma antigen
MAPK	Mitogen activated protein kinase
MCG	Melanoma Cooperative Group (EORTC)
MHC	Major histocompatibility complex
MI	Istituto Nazionale per lo Studio e la Cura dei Tumori, Milano, Italy
MLPC	Mixed lymphocyte-peptide cultures
MPTC	Mixed lymphocyte-tumor culture
MPL	3-deacylated monophosphoryl lipid A
MR	Minor response
MSR	San Raffaele Hospital, Milano, Italy
MTIC	Methyl-triazen-imidazole-4-carboxamide
MxR	Mixed response
MZ	Johannes Gutenberg Universität Mainz, Mainz, Germany
MZP	Mainz, patient

N

NAP	Nantes, patient (Hôtel Dieu, University Hospital, Nantes, France)
NED	No evidence of disease
NK	Natural killer cells
NRH	The Norwegian Radium Hospital, Oslo, Norway
NSCLC	Non-small-cell lung cancer
NW	Krankenhaus Nordwest, Frankfurt am Main, Germany

O

OR	Objective response

P

PBMC	Peripheral blood mononuclear cells
PBS	Phosphate buffered saline
PD	Progressive disease
PR	Partial response
ProtD-MAGE-3-His	Protein D-MAGE-3-Histidine fusion protein

Q

QS21	A saponin extracted from *Quillaja Saponaria Molina*

R

RECIST	Response evaluation criteria in solid tumors
RNA	Ribonucleic acid
RT-PCR	Reverse transcription-polymerase chain reaction amplification

S

SAE	Serious adverse event
s.c.	Subcutaneously
SD	Stable disease
SH	Weston Park Hospital, Sheffield, United Kingdom

T

TAP	Transporter associated with antigen processing
TCR	T-cell receptor
TETp	Precursors of tetramer-labeled cells
TGF	Tumor growth factor
TMZ	Temozolomide
TNF	Tumor necrosis factor
TNM	T, primary tumor; N, regional disease; M, distant metastasis
TOU	Centre Claudius Regaud, Toulouse, France
Treg	Regulatory T cell
TSTA	Tumor specific transplantation antigen

U

UCL	Université catholique de Louvain, Louvain-la-Neuve, Belgium
UHL	University Hospital of Linköping, Linköping, Sweden
UK	Unknown
UKBF	University Hospital Benjamin Franklin, Free University of Berlin, Berlin, Germany
ULB	Université libre de Bruxelles, Brussels, Belgium
UVR	Ultra violet radiations
UZG	Universitair Ziekenhuis Gent, Ghent, Belgium

V

VEGF	Vascular endothelial growth factor
VUB	Vrije Universiteit Brussel, Brussels, Belgium

W

WHO	World Health Organization

SUMMARY

Although melanoma accounts for only 4% of skin cancers, it is responsible for 80% of deaths from skin cancers and its incidence in Caucasians has been increasing steadily during the last 30 years. So far, no treatment - except surgery at the earliest stages of the disease - has been shown to significantly improve survival. New treatments are thus clearly needed. The interest of immunologists for melanoma is based on particular features of this tumor. Rare spontaneous regressions have been described, which are possibly mediated by immune responses. Moreover, melanoma cell lines are relatively easy to obtain, providing essential tools for laboratory studies. The first melanoma vaccines involved inoculations of patients with autologous or allogeneic melanoma cells, as well as a variety of immunological adjuvants. Since the beginning of the nineties, the identification of antigens recognized on human tumors by autologous T lymphocytes has opened the way for new vaccination strategies involving molecularly defined tumor antigens.

An important group of antigens recognized by T lymphocytes is encoded by "cancer-germ line genes", which are expressed in tumors of various histological types, but are silent in normal tissues, with the exception of testis germinal cells and placental trophoblast. Since the latter do not express the HLA molecules required to present these antigens to the T lymphocytes, cancer-germ line genes encoded antigens are only present on tumors, which should limit the risk of generating autoimmune diseases as a consequence of vaccination. Therefore, these widely shared tumor specific antigens should represent good targets for the development of cancer vaccines.

Our clinical research program of therapeutic vaccinations focuses on antigens encoded by the *MAGE* family of cancer-germ line genes. Most of the patients included in our phase I/II immunization trials had measurable metastatic melanoma. Several MAGE peptides as well as a recombinant MAGE-3 protein have been tested, while several additional trials are ongoing, including immunizations with a recombinant poxvirus coding for 2 MAGE epitopes. No major toxicity was reported. Objective tumor responses have been observed in a minority of patients, mainly those who had regional or distant metastases without visceral involvement and some of them have been complete and long lasting. Although the rate of objective tumor responses observed is low, it is clearly higher than the rate of spontaneous tumor regression observed in melanoma.

Other immunization modes against T-cell defined epitopes are currently being explored by several groups in human clinical trials. Vaccines include peptides presented by class I or class II HLA molecules, proteins given alone or mixed with immunological adjuvants or cytokines, recombinant viral or bacterial vectors, dendritic cells and DNA encoding the antigen. Adoptive transfer of T lymphocytes selected for their capacity to recognize defined epitopes presented by the tumor represents another type of approach aiming at the destruction of the tumor by the immune system.

It is difficult to predict whether and when therapeutic vaccination against cancer will reach an efficacy that will be sufficient for a standard cancer treatment. Provided their low toxicity, these vaccines should be tested in an adjuvant setting, at early stages of the disease.