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VRIJE UNIVERSITEIT BRUSSEL

PhD in Medical Sciences
2016-2017

INVITATION to the Public defence of

Sofie WILGENHOF

To obtain the academic degree of **'DOCTOR IN MEDICAL SCIENCES'**

Autologous mRNA electroporated dendritic cell-based immunotherapy for melanoma patients.

Thursday 29 June 2017
Auditorium **Piet Brouwer**, 17:00
Faculty of Medicine and Pharmacy, Laarbeeklaan 103, 1090 Brussel

How to reach the campus Jette:
http://www.vub.ac.be/english/infoabout/campuses

Summary of the dissertation

Dendritic cells are the most professional antigen-presenting cells of the immune system. They play a crucial role in the initiation and regulation of immune responses. Therefore, clinical trials have been conducted, using tumor-antigen loaded dendritic cells as a cellular immunotherapy in cancer patients. The Laboratory of Molecular and Cellular Therapy previously demonstrated that the immunostimulatory capacity of monocyte derived dendritic cells can be greatly enhanced by electroporating immature dendritic cells with messenger RNA encoding for CD40 ligand, CD70 and constitutively active toll-like receptor 4, the so called TriMix formulation. Moreover, these TriMix-DCs can be co-electroporated with melanoma-associated antigens and provide superior antigen-specific T-cell stimulation in vitro.

In this thesis, we evaluated the feasibility, safety, immunogenicity and activity of the autologous TriMixDC-MEL formulation in melanoma patients in three consecutive clinical trials. We demonstrated that TriMixDC-MEL therapy could be succesfully prepared for most of the patients and was well tolerated when injected intradermally. Antigen-specific immune responses were found in half of all patients. Moreover, in melanoma patients at high risk for recurrence after the resection of macrometastases, this therapy resulted in encouraging overall survival compared with historical controls. In a dose-escalation phase I clinical trial we documented anti-tumor responses in pretreated advanced melanoma patients when TriMixDC-MEL was administered intravenously, hereby underlining the importance of the route of administration. Finally, we combined TriMixDC-MEL with an anti-CTLA-4 monoclonal antibody in a phase II study and observed increased efficacy with a high percentage of durable responses in patients with metastatic melanoma.

Curriculum Vitae

Sofie Wilgenhof was born on the 13th of January 1984 in Halle, Belgium. After completing secondary school at the Koninklijk Atheneum Halle, she started as a medical student at the Vrije Universiteit Brussel.

During the last years of medical education she became interested in immunology and medical oncology and in particular in the academic clinical studies with dendritic cell-based immunotherapy led by prof. dr. Bart Neyns and prof. dr. Kris Thielemans at the Vrije Universiteit Brussel and the Universitair Ziekenhuis Brussel. In 2009, she graduated as a Medical Doctor and received a research grant from the Fonds voor Wetenschappelijk Onderzoek Vlaanderen to perform a PhD project at the Laboratory of Molecular and Cellular Therapy (Vrije Universiteit Brussel). During these four years, multiple phase I and II clinical trials with dendritic cell-based immunotherapy were conducted, resulting in the present work and 30 publications (12 as a first author). Sofie presented this work at several national and international meetings and in 2015 she received a grant from the Horlait-Dapsens Foundation to perform a fellowship in Medical Oncology at the Antoni van Leeuwenhoek Ziekenhuis in Amsterdam, the Netherlands. In July 2017 Sofie will finish her training as a Medical Oncologist.