CME Session 13
Translational Molecular Imaging and Therapy + Oncology & Theraonostics Committee
Saturday, October 23, 09:00-10:30

Session Title
Immunotheranostics

Chairperson
Margret Schottelius (Lausanne, Switzerland)

Programme
09:00 - 09:29  Elisabeth G.E. de Vries (Groningen, Netherlands): Immunotherapy and Nuclear Medicine Diagnostics - Where do we Stand?”

09:29 - 09:58  Fernanda Herrera (Lausanne, Switzerland): Combining Immunotherapy and Radiation - Is the Whole more than the Sum of its Parts?

09:58 - 10:27  Niklaus Schaefer (Lausanne, Switzerland): Nuclear Medicine Immunotheranostics - Synergisms and Antagonisms

10:27 - 10:30  Session Summary by Chairperson

Educational Objectives
1. Gain an overview over the currently employed PET imaging approaches to characterize tumours, their tumour microenvironment and local drug trafficking with the aim of predicting response to and overcoming resistance to immunotherapy.
2. Understand the combined effects of low dose external radiation therapy and immunotherapy in the combination treatment of cancer.
3. Get acquainted with the concept of immunotheranostics and sharpen awareness for synergies and antagonisms between immunotherapy and nuclear medicine theranostics.

Summary
Cancer immunotherapy, i.e. the concept of enhancing tumor-specific immunity via e.g. adoptive T-cell transfer, CAR-T cell infusion, immune checkpoint inhibition (PD-1, PD-L1, CTLA-4) or other interventions, has evolved as a very powerful therapeutic approach in clinical oncology and has moved forward at a tremendous pace during the last years. However, only a fraction of the cancer patients undergoing immunotherapy experience long-term remission. This resistance to immunotherapy is based on a highly complex interplay of diverse mechanisms, and molecular imaging using PET is gaining increasing impact in the quest to unravel these mechanisms, to identify the key players and thus to improve therapy outcome.

The questions asked in this context – and the potential answers that can be provided by PET in the setting of immunotherapy (IT) – will be addressed in the first talk. Particular focus will be directed towards the specific characteristics of a given tumor and its influence on drug delivery and distribution as well as the pivotal role of the immune system for successful immunotherapy. So far, IT-PET has shown great value
for predicting patient survival based on the non-invasive assessment of tumor response. Other “puzzle pieces” that are progressively integrated to complete the picture include tumor heterogeneity and its influence on drug distribution and pharmacodynamics within a given lesion and also important factors such as drug dose and target saturation, all of which are crucial parameters for refining and optimizing immunotherapy regimens and to reduce resistance.

One way to overcome or at least weaken this resistance lies in the design of “logical” combination treatments, which invariably aim at breaking down the tumor’s intrinsic defense against the immune system and at increasing the immunogenicity of a given tumor. For example, combining low dose external radiation therapy (LDRT), delivered to large treatment fields, and immunotherapy has shown promising results, both in preclinical and in first clinical studies in ovarian cancer patients. LDRT was shown to reprogram the microenvironment of immune desert tumors, and to enable T-cell homing, rendering tumors responsive to combinatorial immunotherapy. These findings have already been translated into a phase I clinical trial, and its results will be presented in the second talk.

In this context, the next logical step is to exploit and maybe even improve these effects by implementing nuclear medicine-based theranostics in immunooncology (“immunotheranostics”). By making use of the availability of highly specific targeted tracers, this approach, presented in the third presentation, encompasses both the initial visualization and the subsequent targeted attack against the respective line of defense in the local tumor microenvironment and in distant immune compartments. Of course, the goal of such an approach is to optimally exploit synergies between immunotherapy and nuclear medicine theranostics. To realize this, however, a profound understanding of potential synergistic and antagonistic effects of both therapy approaches is required. Furthermore, the question of how to integrate such combination treatment approaches into future oncology/immunotherapy trials and procedures needs to be addressed early on and will be discussed.

**Key Words**

Immunotherapy, PET, combination treatment, radiation therapy, abscopal effect, synergy, antagonism, immunotheranostics