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Randomized, open-label phase III study to evaluate the adjuvant vaccination with tumor RNA-loaded autologous dendritic cells versus observation of patients with resected monosomy 3 uveal melanoma

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Accumulating evidence suggests that T cells recognizing mutated cancer antigens are crucial for successful cancer immunotherapy. They seem to represent the common mechanistic pathway to control tumors and prolong overall survival in active antigen-specific (vaccination) as well as passive antigen-non-specific (checkpoint blockade) therapies. Dendritic cells (DC) besides mutated antigens are the other key to develop better T-based vaccines. Our group has systematically developed the adoptive transfer of these monocyte-derived DC for cancer vaccination loaded with antigens in form of peptides or RNA transfection. In lately secluded trials, high immunogenicity and long-term clinical benefit correlating with certain biomarkers in blood (including simple ones such as eosinophilia) became evident. Using autologous tumor RNA for loading of dendritic cells has the advantage of using not only patient unique mutations as antigens but also the abnormal ligandome generated by abnormal splicing und processing inherent in malignant cells. Following preclinical work and evidence for clinical efficacy in metastatic melanoma, we have started a randomized phase III (NCT01983748) trial in high risk (monosomy 3) uveal melanoma using RNA-transfected DC to vaccinate against the total antigenic repertoire of patient´s individual tumors to retard or prevent metastases after resection of the primary tumor in the eye. A total of 200 patients are randomized into arm A (DC vaccination) or arm B (observation as standard of care). Twenty million mature, monocyte-derived DC loaded with autologous tumor RNA are administered respectively at eight vaccination time points over two years. Objectives are to: Prolong DFS; prolong OS and; induce and measure immune responses. The trial has been started in 2014 and is currently performed in cooperation with Departments of Ophthalmology at eight University Hospitals in Germany (Erlangen, Essen, Hamburg Eppendorf, Homburg/Saar, Köln, Lübeck, Tübingen, and Würzburg).

Biography

Beatrice Schuler-Thurner is a Dermatologist and has profound experience in the guidance of a GMP facility. She has a plethora of experience in performing investigator initiated clinical trials with peptide-loaded and RNA transfected dendritic cells.

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