Universiteit
Leiden
The Netherlands

Defining optimal oncolytic virus treatment and diagnostics in high risk melanoma patients

Stahlie, E.H.A.

Citation

Stahlie, E. H. A. (2023, April 19). *Defining optimal oncolytic virus treatment and diagnostics in high risk melanoma patients*. Retrieved from https://hdl.handle.net/1887/3594222

Version:	Publisher's Version
License:	Licence agreement concerning inclusion of doctoral thesis in the Institutional Repository of the University of Leiden
Downloaded from:	https://hdl.handle.net/1887/3594222

Note: To cite this publication please use the final published version (if applicable).

CHAPTER 10

Summary

In **chapter 2** we set out to identify prognostic factors for achieving a complete response that can be used to optimize patient selection for T-VEC monotherapy. 93 patients with injectable stage IIIB-IVM1a melanoma with a follow-up time >6 months were included. This study demonstrates that T-VEC is able to achieve high complete and durable responses. Tumor size, type of metastases, prior treatment with systemic therapy and stage (8th AJCC) were independent prognostic factors for achieving CR. A prediction model showed that use of T-VEC in patients with low tumor burden is associated with better outcomes, suggesting use earlier in the course of the disease.

The study in **chapter 3** focuses on externally validating the prediction model from chapter 5, in an independent, American patient cohort (n=71). A second nomogram was built incorporating the same predictive factors: tumor size (diameter of largest metastasis), type of metastases (cutaneous, subcutaneous and nodal) and number of metastases (cut-off:<20 & >20). The original model as well as the validation model show comparable and good predictive accuracy. The validation model reinforces the conclusion that for the best response to T-VEC, it should be used early on in the course of the disease, when the tumor burden is cutaneous with smaller diameter and fewer of metastases.

Chapter 4 is a systematic review and meta-analysis investigating the efficacy- and safety outcomes of single agent T-VEC in stage IIIB-IVM1c melanoma patients. Eight studies with a total of 642 patients were included. Our results show that patients with early metastatic disease (stage IIIB-IVM1a disease) achieve superior response rates to single agent T-VEC treatment than patients who also harbor distant visceral metastases (stage IVM1b-c). Besides, T-VEC is well tolerated with generally only mild toxicities.

Chapter 5 describes the false positive FDG uptake in melanoma patients treated with T-VEC. In a Dutch cohort (n=137), almost one-third of patients developed new-onset FDG uptake in uninjected locoregional lymph nodes during T-VEC. In 68% of these patients, lesions were classified as "suspected metastases", which in the majority of patients (75%) was nog confirmed by pathological examination or routine follow-up. These false positive results indicate that new-onset FDG uptake in locoregional lymph nodes during T-VEC treatment does not necessarily reflect progressive disease, but may be associated with immune infiltration. Therefore, it is recommended to obtain representative tissue.

Chapter 6 is a prospective feasibility study investigating the role of dermoscopy in monitoring the response of cutaneous melanoma metastases (CMM) to T-VEC. In six patients, a total of 11 CMM were selected: macroscopic as well as dermoscopic pictures were taken at baseline, prior to each treatment with T-VEC and prior to

histological biopsy. The pictures were evaluated by two investigators, using a color-based pattern classification. Metastases with a pink pattern showed changes on a dermoscopic that were not also seen on a macroscopic level, while all remaining metastases did not show these changes. This suggests for CMM with a pink pattern, dermoscopy can provide additional information regarding the response to T-VEC. For cutaneous metastases with a blue, brown or a mixed pattern, dermoscopy does not provide additional information on top of the information obtained through physical examination and macroscopic lesion photography.

In **chapter 7** we describe the role of surveillance imaging in high-risk stage III melanoma patients after complete surgical resection of disease. Patients were divided over two cohorts: cohort 1 (n=35) focused on surveillance in asymptomatic patients and patients were assigned to one FDG-PET/CT every 6 months for 2 years, with one final scan after 3 years; cohort 2 (n=42) focused on screening between surgery and before start of adjuvant therapy, so patients were assigned to one screening FDG-PET/CT. With 12 asymptomatic recurrences detected by FDG-PET/CT in cohort 1, we demonstrated that surveillance with 6-monthly FDG-PET/CT scans after complete surgical resection of stage IIIB/C melanoma has a high sensitivity and specificity, although with a broad confidence interval, for detecting asymptomatic recurrence and a high NPV and PPV. In cohort 2, up to 9.5% of patients had recurrences detected by FDG-PET/CT, leading to alterations in therapy. This study shows that FDG-PET/CT is a valuable imaging tool to detect recurrence in stage III melanoma, even shortly after surgery.

Chapter 8 describes the results of a pilot study (n=23) that we undertook to assess the value of ultrasound and FDG-PET/CT prior to lymphoscintigraphy and SLNB for stage IIB/C melanoma patients. Ultrasound detected metastases in 22% of patients, altering their treatment and preventing unnecessary surgery, which suggests it is effective in the work-up of stage IIB/C melanoma. However, 8 (47%) of 17 patients without macroscopic disease, still had a positive SN. Therefore, preoperative negative imaging does not exclude the presence of SN metastases and SLNB cannot be foregone. Staging with FDG-PET/CT is not of added value prior to LSG and SLNB and should therefore not be used.