Goedgekeurde aanvraag gegevens ten behoeve van wetenschappelijk onderzoek

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Titel onderzoek
Real-world treatment sequences and outcomes in patients with advanced cutaneous melanoma in The Netherlands

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Beschrijving onderzoek
The impact of novel treatments on progression and survival for patients with advanced cutaneous melanoma in The Netherlands is likely to differ between trial populations and real-world patients. An important reason for this is greater patient and treatment heterogeneity in clinical practice. For instance, RCT’s often exclude patients with brain metastases and a low performance status while these patients may receive treatment in clinical practice. More importantly, RCTs most often only compare two different treatments whereas in clinical practice patients receive different types of treatments as well as multiple treatment in different sequences. Due to prolonged survival of patients with advanced melanoma, it is likely that the number of treatments a patient receives will further increase in the future. However, not much is known how a treatment sequence and treatment history may affect disease progression and survival.

Statistiek
We will first use descriptive statistics for analyzing the types of treatment and the treatment sequences. To estimate time to next treatment and survival we will fit parametric multi-state models (common used modelling methods in health economics) to the DMTR data (Putter, H., Fiocco, M. and Geskus, R. B. (2007), Tutorial in biostatistics: competing risks and multi-state models. Statist. Med., 26: 2389–2430. doi:10.1002/sim.2712). Employing parametric models rather than non-parametric models (such as Cox survival models) allow to estimate mean survival and time to next treatment rather than just median survival/time to next treatment. Furthermore, the use of parametric models allows to predict in scenarios what 2017.1
would happen beyond the follow-up time observed in the DMTR. States in the multi-state model will be distinguished based on treatment categories (chemotherapy, immunotherapy and targeted therapy) and the absorbing state death. Patient and tumor characteristics such as gender, performance status, LDH level, brain metastases, and BRAF mutation will be used as time invariant covariates. Depending on the model specification and the observed treatments and sequences in the DMTR, the number of treatment lines and the sequences will be entered as a time-varying covariate. Aim of the analysis is to evaluate the extent to which the number of treatments received and the applied sequences have an impact on time to next treatment and survival across treatment categories and/or whether there are interactions. With the estimated models we will carry out scenario analyses exploring the impact of different treatment sequences on disease progression and survival. Model selection will be based on a combination of clinical expertise and statistical criterion such as the Akaike Information Criterion.

**Beoogde publicatie**
Real-world treatment sequences and outcomes in patients with advanced cutaneous melanoma in The Netherlands.