Melanoma is the cancer with highest likelihood to develop brain metastases. Due to the blood-brain barrier medicinal treatment is limited and overall survival of these patients usually does not exceed 6 months from date of diagnosis of brain metastases. Therefore in most clinical trials patients with brain metastases were excluded. However, there were hints that immunotherapy has a positive effect on brain metastases. This is why within this clinical trial, patients with active brain metastases were enrolled prospectively. It was planned to register 68 patients. Between March 2018 and May 2019, 8 patients were screened, of these 6 patients were enrolled. Due to slow recruitment the study was prematurely discontinued in June 2019.

No analysis of primary and secondary endpoints was possible due to rapid progression of disease leading to death of 5 patients. None of the patients had the planned second imaging method besides the examination at baseline performed.

In an open-label phase II trial enrolling melanoma patients with asymptomatic and symptomatic brain metastases it was shown that treatment with four doses of 10 mg/kg ipilimumab every 3 weeks was especially effective if brain metastases were small and asymptomatic. In this trial, administration of combination therapy with nivolumab and ipilimumab did not seem to improve activity in patients with 4 and more active brain metastases. This is in line with other results in melanoma patients with brain metastases which demonstrate that immunotherapy may not be very effective in these patients. For example, an updated analysis of the CheckMate 204 trial demonstrated minor efficacy of nivolumab + ipilimumab combination therapy with the same doses as administered in the present trial in patients with symptomatic compared to patients with asymptomatic brain metastases.

However the number of enrolled patients into this prospective clinical trial is too low for final conclusions regarding efficacy in patients with several symptomatic brain metastases, although the results support the importance of starting immunotherapy as early as possible before number of brain metastases is too high for successful treatment.

Regarding safety issues, no unexpected toxicities were reported. This is in accordance with other clinical trials which enrolled melanoma patients with brain metastases and in which also no unknown adverse reactions occurred.