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Early discontinuation of anti-PD-1 therapy upon achieving a complete or partial response in patients with metastatic melanoma: The multicentre prospective Safe Stop Trial

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Background

Anti-PD-1 therapy has significantly improved survival for patients with metastatic melanoma. However, long treatment duration (i.e. ≥ two years) has significant impact on patients, the potential development of (severe) immune-related adverse events (irAEs), health-related quality of life (HRQoL) and healthcare resources. Currently, there is no consensus on the optimal treatment duration. Aim of the Safe Stop Trial was to evaluate whether discontinuation of first-line anti-PD-1 at first confirmation of response is safe in patients with metastatic melanoma.

Methods

The Safe Stop Trial is a nationwide, prospective, single-arm, non-inferiority trial in the Netherlands (PMID 33765967). Patients with irresectable stage III or metastatic melanoma and a confirmed complete response (CR) or partial response (PR) (RECIST v1.1) were included to stop first-line anti-PD-1 monotherapy. In case of disease progression, anti-PD-1 could be restarted. Other salvage therapy was allowed at the discretion of the treating physician. Primary objective was the rate of ongoing responses at 24 months after treatment initiation. This was compared to the ongoing response rate (CR or PR) of 39% at 24 months, reported for all patients who completed 24 months of treatment in the KEYNOTE-006 trial.

Results

Between February 2019 and August 2023, 200 patients were included in all fourteen Dutch melanoma centres. Median treatment duration with anti-PD-1 was 24 weeks (IQR 20-26 weeks). At inclusion in the trial, 58 (29%) patients had CR and 10 (5%) patients were known with brain metastasis. The ongoing response rate at 24 months was 81.8% (90% CI 76.7–85.8%). Overall survival rate at 24 months was 95.9% (90% CI 92.8-97.7%) and melanoma-specific survival at 24 months was 97.4% (90% CI 94.7–98.8%).

Conclusions

The Safe Stop Trial is the first completed prospective trial to evaluate the safety of a shorter duration of anti-PD-1 in patients with metastatic melanoma. Given the high rates of ongoing responses and overall survival after early treatment discontinuation, results of this trial indicate that it is safe to early stop anti-PD-1 in patients with metastatic melanoma who achieve a CR or PR.

Clinical trial identification

The Safe Stop trial has been registered in the Netherlands Trial Register (NTR), Trial NL7293 (old NTR ID: 7502), https://www.trialregister.nl/trial/7293. Date of registration September 30, 2018.

Legal entity responsible for the study

The authors.

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Disclosure

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