Minimal Residual Disease by Circulating Tumor DNA as a Biomarker of Recurrence-free Survival in Resected High-risk melanoma Patients Treated With mRNA-4157 (V940), a Personalized Cancer Vaccine, and Pembrolizumab


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Background

The trial, conducted at baseline ctDNA-evaluable patients with resected stage III melanoma, was a randomized phase III study comparing mRNA-4157 (V940) (n = 125) and pembrolizumab (n = 126) in patients with high-risk melanoma. ctDNA-evaluable patients that were randomly assigned to either mRNA-4157 (V940) + pembrolizumab or pembrolizumab alone were evaluated for MRD at baseline across multiple cancer types. The incidence of MRD in melanoma patients over 4 years was 0.10% in the mRNA-4157 (V940) + pembrolizumab arm and 0.33% in the pembrolizumab arm. The study was designed and stratified by disease stage to detect differences in RFS between the combination and single-agent arms. The study was designed with 80% power to detect an HR of 0.5 with ≥40 RFS events (with a 1-sided alpha of 0.1).

Results

The majority of ctDNA-evaluable patients were female (59%), and the median (range) age was 65 years (29-89). The majority of ctDNA-evaluable patients were female (59%), and the median (range) age was 65 years (29-89). The majority of ctDNA-evaluable patients were female (59%), and the median (range) age was 65 years (29-89). The majority of ctDNA-evaluable patients were female (59%), and the median (range) age was 65 years (29-89). The majority of ctDNA-evaluable patients were female (59%), and the median (range) age was 65 years (29-89). The majority of ctDNA-evaluable patients were female (59%), and the median (range) age was 65 years (29-89). The majority of ctDNA-evaluable patients were female (59%), and the median (range) age was 65 years (29-89). The majority of ctDNA-evaluable patients were female (59%), and the median (range) age was 65 years (29-89). The majority of ctDNA-evaluable patients were female (59%), and the median (range) age was 65 years (29-89). The majority of ctDNA-evaluable patients were female (59%), and the median (range) age was 65 years (29-89). The majority of ctDNA-evaluable patients were female (59%), and the median (range) age was 65 years (29-89). The majority of ctDNA-evaluable patients were female (59%), and the median (range) age was 65 years (29-89). The majority of ctDNA-evaluable patients were female (59%), and the median (range) age was 65 years (29-89). The majority of ctDNA-evaluable patients were female (59%), and the median (range) age was 65 years (29-89). The majority of ctDNA-evaluable patients were female (59%), and the median (range) age was 65 years (29-89). The majority of ctDNA-evaluable patients were female (59%), and the median (range) age was 65 years (29-89).

Conclusions

MRD detection by plasma ctDNA assay at the start of adjuvant melanoma treatment was observed in only 12% of patients in mRNA-4157 (V940)/KEYNOTE-942 but was associated with shorter RFS in those patients. In ctDNA-negative patients, the combination treatment of mRNA-4157 (V940) + pembrolizumab improved RFS compared to pembrolizumab monotherapy.

References


Acknowledgments


[Table 1] Distribution of ctDNA-positive and ctDNA-negative patients at baseline (n=125; 109 vs 45).

[Table 2] Baseline characteristics versus ctDNA-evaluable, ctDNA-positive, and ITT populations; baseline characteristics by treatment arm and RFS.

[Table 3] Prognostic value of baseline ctDNA and other tumor biomarkers in patients with resected high-risk melanoma.

[Figure 1] mRNA-4157 (V940)-P201/KEYNOTE-942 trial study design.

[Figure 2] Improved RFS in ctDNA-negative patients at baseline treated with a combination of mRNA-4157 (V940) + pembrolizumab compared to pembrolizumab monotherapy.

[Figure 3] ctDNA status at baseline has prognostic value in patients with resected high-risk melanoma.

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