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Rescuing cancer immunotherapy with plasma exchange in melanoma (the ReCIPE-M1 study)

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Background

Immune checkpoint inhibitors (ICI) are initially effective in metastatic melanoma and other advanced cancers. ICI-refractory cancers are fatal. There is a critical need to better understand and combat ICI resistance. We and others have shown that soluble PD-L1 (sPD-L1) and other circulating immunosuppressive factors drive ICI resistance. We previously showed that therapeutic plasma exchange (TPE) removes sPD-L1 from circulation. We hypothesized that TPE and ICI re-challenge may re-sensitize melanomas to ICI therapy.

Methods

34 patients with ICI-refractory melanoma were screened. 18 patients with sPD-L1 ≥1.7 ng/mL underwent three sessions of TPE (once daily for three days) to clear sPD-L1 and ICI re-challenge. Primary endpoints were adverse events and sPD-L1 reduction. Secondary endpoints included overall survival (OS), response, and progression-free survival. Correlative studies were performed on circulating factors and immune cell subsets.

Results

The overall response rate was 61% (11/18), with multiple patients enjoying yearslong disease-free survival. We previously reported that OS was predicted by the level and duration of suppression of sPD-L1. We have further found other circulating immune factors at ICI2 predict overall survival. Inferior survival is predicted by surging levels of CD84 (HR 27.6, p=0.003), IL1α (HR 18.7, p=0.013), IL1 β (HR 4.7, p=0.028), and IL18 (HR 7.5, p=0.016). Superior OS is predicted by surging levels of *Wnt* signaling inhibitors (HR 0.1, p=007) and complement (HR 0.012, p=0.02). In extended follow-up, OS was favorable for patients with increasing anti-tumor immune cell subsets that correlated with changes in circulating soluble factors.

Conclusions

In extended follow-up, TPE and ICI re-challenge were associated with significant response and duration of response that compare favorably with landmark studies of ICI monotherapy re-challenge or ICI switch. Additional data show that the suppression of multiple additional circulating factors further predict outcomes. Our study is limited as a single-arm trial with radiotherapy to a minority of lesions, which limits interpretation. Additional randomized trials are ongoing. These findings support additional ongoing clinical trials.

Clinical trial identification

NCT04581382 (ReCIPE-M1).

Legal entity responsible for the study

Mayo Clinic.

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Disclosure

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