Impact of previous immunotherapy on chemotherapy efficacy in metastatic melanoma

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Introduction

- Metastatic melanoma is a highly malignant neoplasm. There are differences in the treatment of melanoma between races. Immunotherapy has been shown to be effective in Caucasians, but for Asian patients with MM and ALM, current immunotherapy has been difficult to meet the need for recovery.
- Chemotherapy is widely used in the treatment of diseases, and albumin-bound paclitaxel (nab-ptx), an albumin-based drug, is currently an emerging chemotherapy regimen due to its ability to guide tumor cells with high precision.
- Therefore, the current study sought to investigate whether immunotherapy administered prior to chemotherapy in Asian patients with metastatic melanoma facilitates the efficacy of subsequent chemotherapy, differentiating between immunotherapy regimens and timing.

Materials and Methods

Study Design

- In this study, 1,224 patients with malignant melanoma who received chemotherapy at Zhejiang Cancer Hospital between 2016.1.1 and 2021.12.31 were screened. The study design is shown in Figure 1..

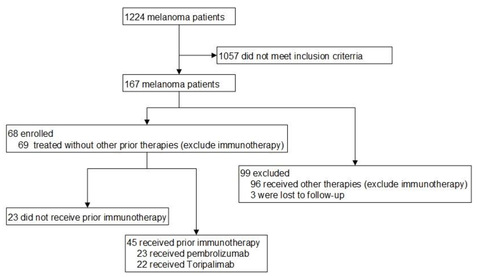


Figure 1 Study design, screening, and enrollment of the participants

Study Participants

- **Inclusion criteria**: (1) Age ≥ 18 years; (2) Patients with unresectable or metastatic melanoma confirmed by histopathology or cytology; (3) Patients whose lesions can be assessed as target lesions (at least one measurable lesion) according to the Response Evaluation Criteria in Solid Tumours (RECIST) guidelines (version 1.1).
- **Exclusion criteria**: (1) Patients with a history of other malignancies within the past 3 years were excluded; (2) Patients with life-threatening cardiovascular disease were excluded.

Statistical Analysis

- Overall survival (OS) and Progression-Free Survival (PFS) were measured from the start of chemotherapy to the date of death or disease progression, and descriptive summaries were performed using Kaplan Meier survival analysis and log-rank tests to compare the groups. A Cox model was used for the risk ratio (HR) with a 95% confidence interval.

Results

Patient characteristics

The average age of the 68 patients was 58 years, and the most prevalent melanoma subtype among the patients was statistically the marginal type, followed by the non-chronic sun damaged type and the mucosal type, and following progression, the majority of patients had melanoma metastases to distant lymph nodes or to the lungs.

In the data on the patients' mutations, 6 (8.82%) had BRAF mutations, 12 (17.65%) had NRAS mutations and 4 (5.88%) had KIT mutations. The majority of the patients had higher than normal serum lactate dehydrogenase (LDH) activity. In addition, 45 of the 68 chemotherapy patients had received immunotherapy (IMT) prior to chemotherapy and 23 had not received immunotherapy (non-IMT) during the study period..

non-IMT and IMT

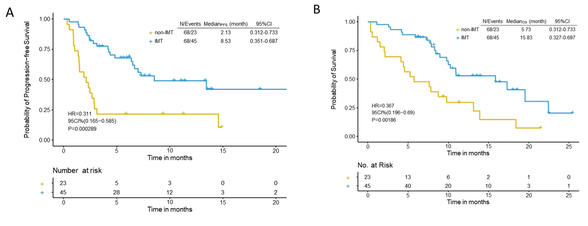


Figure 2 Survival rates in the IMT and non-IMT groups. (A) Kaplan-Meier assay for progression-free survival. (B) Kaplan-Meier assay for overall survival. p<0.05 indicates a statistically significant difference.

- Thenon-IMT group had a higher progression or mortality rate than the IMT group. And there was a significant difference in median PFS between the two groups, with a longer median PFS in the IMT group than in the non-IMT group (Figure 2A).
- In addition, 6-month PFS was estimated to be 21 % in the non-IMT group compared to 68 % in the IMT group. At the time of final OS analysis, there was a significant difference in median OS between the two groups, with a median OS of around 5.5 months in the non-IMT group and around 16 months in the IMT group (Figure 2B).

Toripalimab Injection and Pembrolizumab

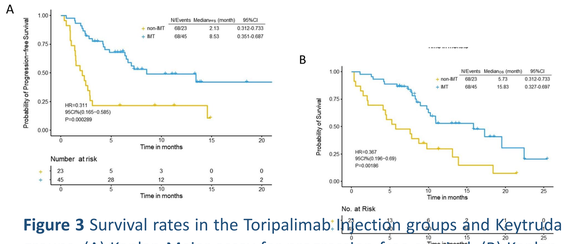
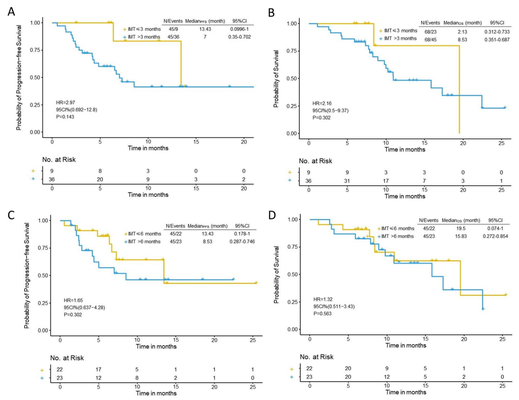


Figure 3 Survival rates in the Toripalimab Injection groups and Keytruda groups. (A) Kaplan-Meier assay for progression-free survival. (B) Kaplan-Meier assay for overall survival. p<0.05 indicates a statistically significant difference.

- Immunotherapy patients were divided into two groups according to the drug used for immunotherapy. After undergoing PFS analysis, there was no significant difference in PFS between the two groups (Figure 3A).
- After the final OS analysis, there was no significant difference in OS between the two groups (Figure 3B). It is thus clear that the drugs used for immunotherapy had no effect on subsequent chemotherapy.

Duration of immunotherapy (3 months or 6 months)



- Patients were divided into two groups according to whether the duration of immunotherapy was longer than 3 months.After PFS analysis, there was no significant difference in PFS between the two groups (Figure 4A). After the final OS analysis, there was no significant difference in OS between the two groups (Figure 4B).
- Patients were divided into two groups according to whether the duration of immunotherapy was longer than 6 months. After PFS analysis, there was no significant difference in PFS between the two groups (Figure 4C). After the final OS analysis, there was no significant difference in OS between the two groups (Figure 4D).

Figure 4 Survival rates in the IMT <3 months group, IMT >3 months group, IMT <6 months group and IMT >6 months group. (A) Kaplan-Meier assay for progression-free survival in the 3-month group. (B) Kaplan-Meier assay for overall survival in the 3 months group. (C) Kaplan-Meier assay for progression-free survival in the 6 months group. (D) Kaplan-Meier assay for overall survival in the 6 months group. p<0.05 indicates a statistically significant difference.

Conclusion

- In summary, this study demonstrates that Asian patients with metastatic melanoma who received chemotherapy after immunotherapy had a better prognosis and that the timing and regimen of immunotherapy had no effect on subsequent chemotherapy. However, in order to further explore the effect of chemotherapy after immunotherapy on metastatic melanoma in Asians, studies in populations from more Asian countries and continuous optimization of treatment regimens are needed.

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Additional Information

Ethics Statement

- The study was approved by the Ethics Committee of Zhejiang Cancer Hospital and all patients signed a written informed consent.

Funding

- This study was supported by National Natural Science Foundation of China (81702653 to J.C).

Funding Conflict of Interest

- The authors declare that there is no conflict of interest regarding the publication of this paper.