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Real-world outcomes of adjuvant therapy in melanoma: an Italian referral center experience.

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Introduction

Adjuvant therapy, encompassing immune checkpoint inhibitors (ICI) and targeted therapies (TT), has demonstrated enhanced prognosis for stage III and IV-NED melanoma patients in numerous clinical trials. Nevertheless, the evaluation of real-world outcomes and the impact of prognostic factors on patient outcomes remains essential. This study aims to assess the real-world effectiveness of adjuvant therapy in terms of relapse-free survival (RFS), distant metastasis-free survival (DMFS), and overall survival (OS).

Materials and methods

This retrospective analysis encompassed 163 disease-free stage III/IV-NED melanoma patients who received targeted therapy (dabrafenib/trametinib) or immunotherapy with ICI (nivolumab, pembrolizumab) for up to 12 months at the University of Turin. TT and pembrolizumab were administered for stage III, while nivolumab was suitable for stage III and IV-NED.

Results

Of the patients, 82 (50.3%) underwent TT, and 81 (49.7%) received ICI. At the 45-month assessment, the overall RFS was 59% (fig.1), with figures of 57.6% for TT and 63.9% for nivolumab. Pembrolizumab exhibited a 38-month RFS of 27.1% (p=0,628). In terms of DMFS at 45 months (fig.2), the overall rate stood at 76.2%, split between 75.6% for TT and 78.9% for nivolumab. Pembrolizumab demonstrated a 38-month DMFS of 50.2% (p=0,960). The overall OS at 45 months was 63.9% (fig.3), with 68.3% for TT and 75.3% for nivolumab. Pembrolizumab displayed a 38-month OS of 46.7% (p=0,724).

Total lymph-node dissection (TLND) was performed in 52.1% of the patients and its impact on RFS, DFMS, and OS was insignificant in univariate and multivariate analysis. Multivariate Cox models underscored the influence of ulceration (p=0,048), stage (p=0.018), and metastasis size (p=0,021) on recurrence probability. Ulceration also exerted significant influence on distant metastasis development (p=0,031) and mortality probability (p=0.021). Overall, 68.3% of patients on TT and 13.6% on ICI temporarily halted treatment due to adverse events, whilst more ICI-treated patients permanently discontinued treatment due to adverse events compared to TT(14.8% vs. 11.1%).

Fig.2

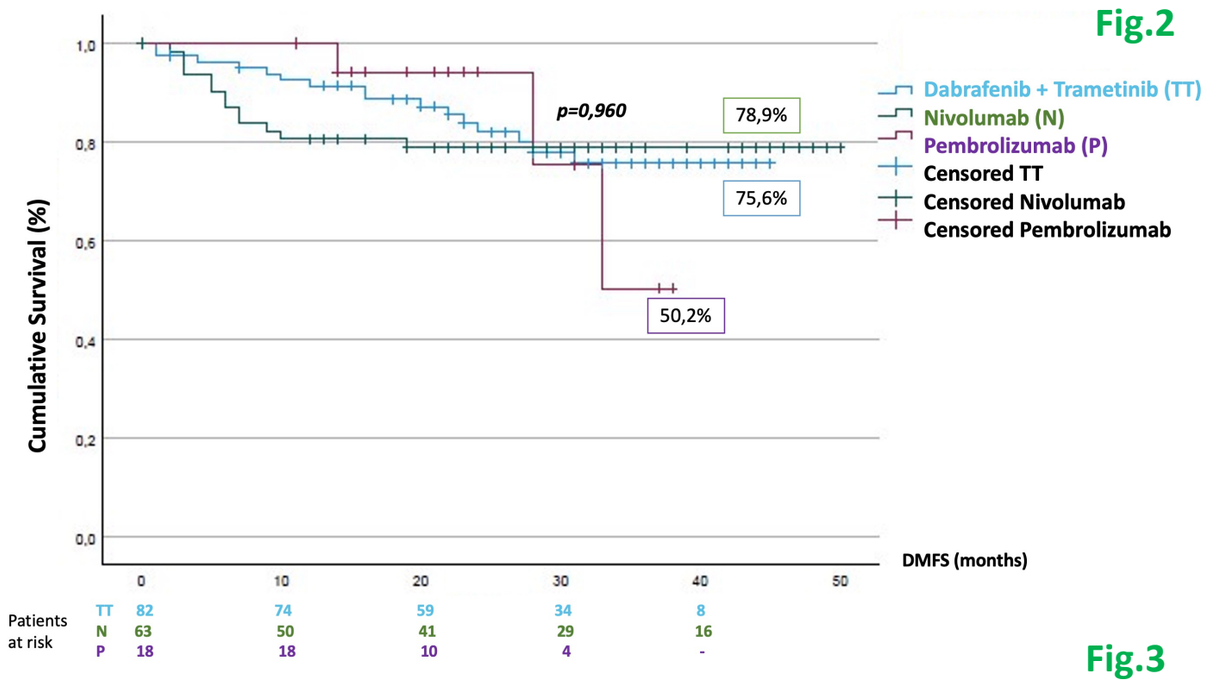


Fig.1

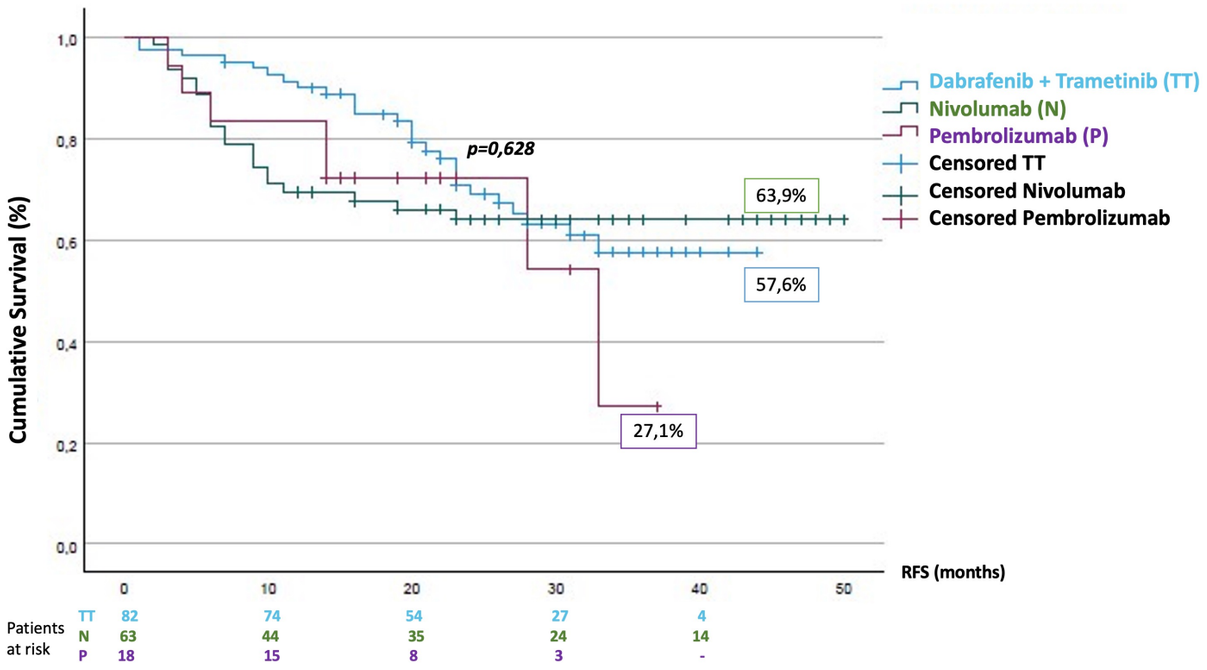
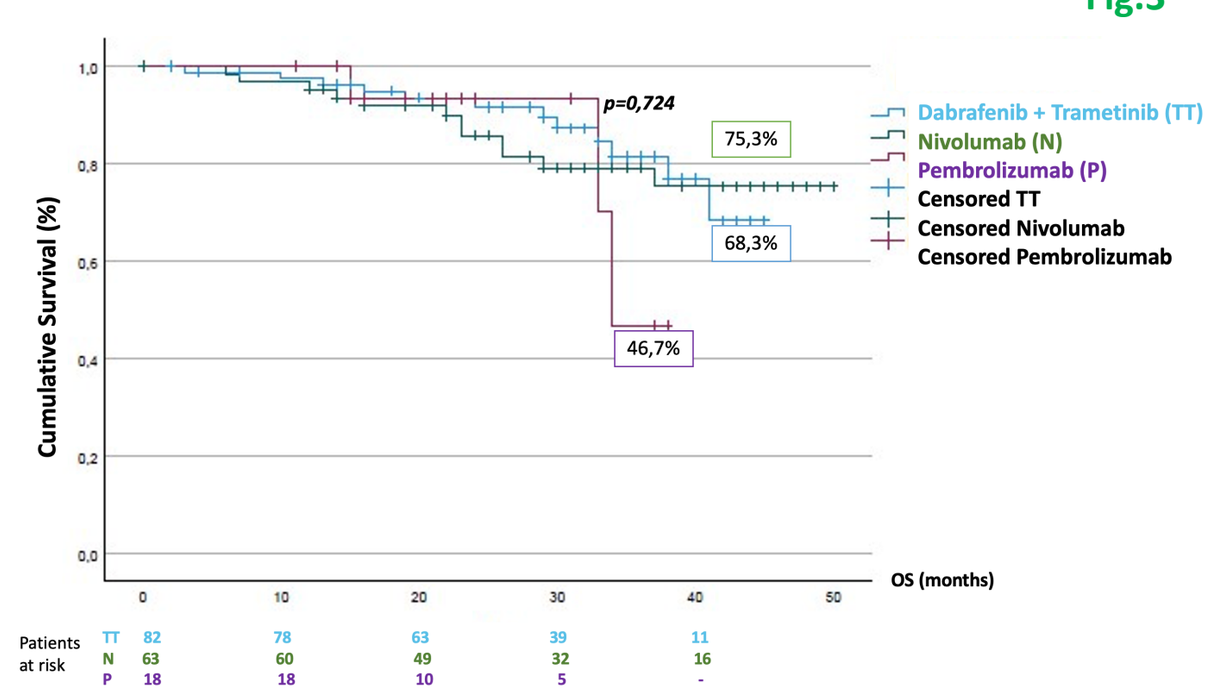


Fig.3



Discussion

Both ICI and TT demonstrate real-world validation of the improvements observed in clinical trials, with no significant differences between the two categories. The lower survival rates observed in the pembrolizumab group can likely be attributed to its smaller sample size. Overall, differences in recurrence patterns and locations have emerged, as ICI-treated patients experienced higher relapse rates during treatment, while TT-treated patients relapsed more frequently off-treatment. Pulmonary recurrence was more prevalent in ICI-treated patients, whereas TT-treated patients saw higher rates of brain metastasis. At last, our study confirms that lymph-node dissection does not have a significant impact on survival in stage III patients with positive sentinel lymph node biopsy.

References

1. Ascierto PA et al. Adjuvant nivolumab versus ipilimumab in resected stage IIIB-C and stage IV melanoma (CheckMate 238): 4-year results from a multicentre, double-blind, randomised, controlled, phase 3 trial. *Lancet Oncol*. 2020;21(11):1465-1477.
2. Eggermont AMM, et al. Adjuvant Pembrolizumab versus Placebo in Resected Stage III Melanoma. *N Engl J Med*. 2018;378(19):1789-1801.
3.Long GV et al. Adjuvant Dabrafenib plus Trametinib in Stage III BRAF-Mutated Melanoma. *N Engl J Med*. 2017;377(19):1813-1823.