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# Response and survival in in-transit metastatic unresectable melanoma according to treatment strategy

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### Background

There is no consensus on the optimal treatment for patients with unresectable melanoma in-transit metastases (ITM). This study describes response and survival outcomes of different treatment strategies for ITM.

### Methods

Patients diagnosed with unresectable ITM with or without lymph node metastases (stage III or IV M1a) from January 2013 to June 2025, were included from the nationwide Dutch Melanoma Treatment Registry (DMTR). We analysed objective response rate (ORR), progression-free survival (PFS), and overall survival (OS). A multivariable Cox proportional hazards model was performed to adjust for confounding factors: age, sex, WHO performance status, LDH level, and nodal disease.

### Results

A total of 458 patients were included: 212 received first-line anti-PD1 (aPD1), 179 T-VEC, and 67 BRAF(/MEK) inhibition (BMi). Patients treated with T-VEC less often had stage IV-M1a disease and more often had ITMs without nodal involvement. ORR was 55.2% for aPD1, 54.7% for T-VEC, and 67.2% for BMi. Median PFS was 7.8 months (95%CI 5.7-13.8) for aPD1, 5.9 months (95%CI 4.3-7.5) for T-VEC, and 8.5 months (95%CI 6.9-14.3) for BMi. Median OS was 38.7 months (95%CI 32.4-64.7) for aPD1, not reached for T-VEC, and 24.7 months (95%CI 17.0-60.0) for BMi. When separately analyzing patients without nodal disease in all 3 treatment groups, OS for T-VEC remained significantly better than for BMi ($p<0.001$) or aPD1 ($p=0.001$). However, multivariable Cox regression for PFS demonstrated no significant difference in the hazard of progression or death for BMi ($HR_{adj}$: 1.00, 95%CI: 0.62–1.60, $p=0.992$) or aPD1 ($HR_{adj}$: 1.00, 95%CI: 0.66–1.51, $p=0.996$) compared to T-VEC. Similarly, multivariable Cox regression for OS did not find a significant difference in hazard of death for BMi ($HR_{adj}$: 1.84, 95%CI: 0.97-3.50, $p<0.200$) or aPD1 ($HR_{adj}$: 1.49, 95%CI: 0.81-2.73, $p=0.062$) compared to T-VEC.

### Conclusions

For ITM unresectable melanoma, aPD1, T-VEC, and BMi-based treatments can induce clinically meaningful responses. After adjusting for potential confounding factors PFS and OS were comparable across patients receiving aPD1, TVEC or BMi.

### Legal entity responsible for the study

The authors.

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