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# Efficacy and safety of RP1 plus nivolumab in patients with advanced anti–PD-1-failed acral melanoma

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### Background

Acral melanoma is a rare and aggressive type of melanoma (2%–3% of all cases) that often has poor outcomes. Acral melanoma responds poorly to available therapies, such as immune checkpoint inhibitors, particularly after progression on first-line treatment. RP1 (vusolimogene oderparepvec) is an oncolytic immunotherapy expressing human granulocyte-macrophage colony-stimulating factor and a fusogenic glycoprotein (GALV-GP-R$^-$). RP1 + nivolumab (nivo) demonstrated an ORR of 32.9% by blinded independent central review (BICR) using RECIST 1.1 in patients (pts) with anti–PD-1–failed advanced melanoma from the IGNYTE trial (NCT03767348). Here we report an ad hoc analysis of RP1 + nivo efficacy and safety in pts with acral melanoma.

### Methods

The IGNYTE phase 2 registrational cohort enrolled pts with stage IIIB–IV cutaneous melanoma and confirmed progression on anti–PD-1 ± anti–CTLA-4 for ≥8 weeks as the last prior treatment (N = 140). RP1 was administered intratumorally at $1 \times 10^6$ plaque-forming units (PFU)/mL initially, then at $1 \times 10^7$ PFU/mL Q2W (≤7 doses) with intravenous nivo.

### Results

Of 140 pts with anti–PD-1–failed cutaneous melanoma, 18 (12.9%) had acral melanoma. Of these 18 pts, 50.0% (9/18) had stage IVM1b–d disease, 94.4% (17/18) had *BRAF* wild-type tumors, and 72.2% (13/18) had PD-L1–negative (<1%) tumors. Most pts (61.1% [11/18]) had both anti–PD-1 and anti–CTLA-4 prior treatment, and 72.2% (13/18) had primary resistance to anti–PD-1. Following treatment with RP1 + nivo, the confirmed ORR was 44.4% (8/18) by BICR using RECIST 1.1, including 16.7% (3/18) complete response and 27.8% (5/18) partial response. Median (95% CI) duration of response was 11.9 (3.6–NR) months (ongoing). Most treatment-related adverse events (TRAEs) were grade 1/2; the most common TRAEs (any grade) were chills, pyrexia, fatigue, injection-site pain, and nausea. Grade ≥3 TRAEs were reported in 2 (11.1%) pts.

### Conclusions

RP1 + nivo demonstrated deep and durable efficacy and was well tolerated in pts with advanced anti–PD-1–failed acral melanoma. RP1 + nivo represents a promising treatment approach for this rare, aggressive melanoma subtype.

## Clinical trial identification

NCT03767348.


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