# LBA9519: Ipilimumab and Nivolumab plus UV1, an Anticancer Vaccination Against Telomerase, in Advanced Melanoma

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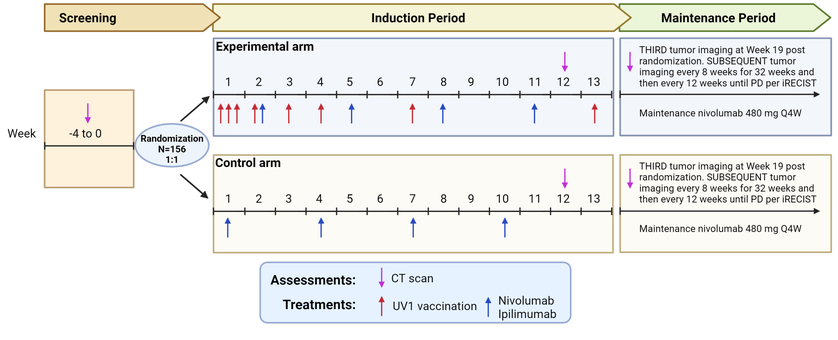
## INTRODUCTION

The combination of ipilimumab (IPI) and nivolumab (NIVO) remains a standard of care for patients with advanced melanoma, especially those with poor prognostic factors, albeit with a significant risk of toxicity. Therapeutic cancer vaccines are ideally positioned to improve outcomes without significantly increasing toxicity. UV1 is a therapeutic cancer vaccine generating T-cell responses against the universal cancer antigen telomerase. The vaccine has been shown to induce persisting anti-telomerase T cell responses of the Th1 CD4+ phenotype that is hypothesized to strengthen and broaden the overall anti-tumor T cell response, an apparent bottleneck for greater efficacy from checkpoint inhibition. In a Phase I trial in melanoma (N = 30), UV1 plus pembrolizumab demonstrated a tolerable safety profile, a complete response rate of 33%, median PFS of 18.9 months, and 2-year OS rate of 73.3%. Recently, results from a randomized Phase II trial indicated a longer overall survival and a higher response rate for previously treated patients with advanced mesothelioma receiving UV1 in combination with IPI-NIVO (Haakensen et al, Eur J Cancer 2024).

## METHODS

In this Phase II, open-label, multicenter study, we randomly assigned treatment-naïve patients with unresectable or metastatic melanoma (stage IIIb-IIId or IV) to IPI 3mg/kg + NIVO 1mg/kg for 4 cycles, followed by NIVO 480 mg as maintenance, with or without 8 intradermal injections of 300 µg UV1 (+GM-CSF). The primary endpoint was progression-free survival (PFS) assessed by blinded independent central review (BICR) according to RECIST 1.1. Secondary endpoints included overall survival (OS), objective response rate (ORR), duration of response, and safety.

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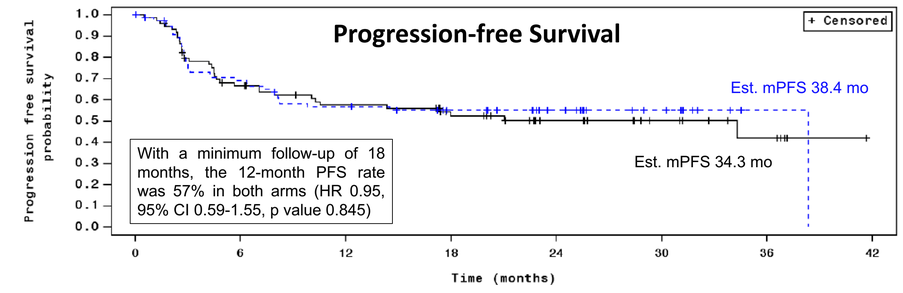
## RESULTS

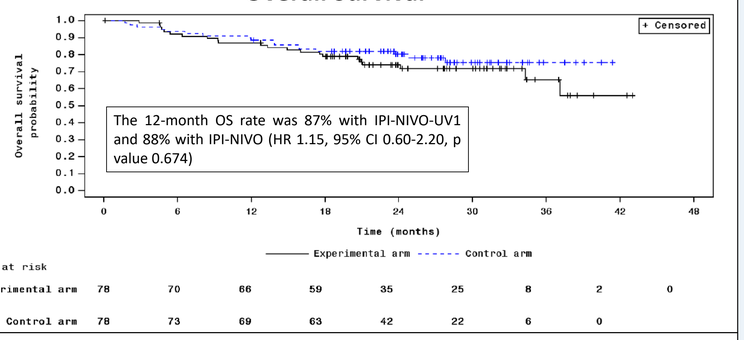
### Baseline Demographics

| | Ipilimumab-nivolumab-UV1 (n=78) | Ipilimumab-nivolumab (n=78) |
|---|---|---|
| Median age (range) — yr | 62.5 (30 to 83) | 58.0 (27 to 88) |
| Female sex — no. (%) | 25 (32.1%) | 29 (37.2%) |
| **ECOG PS score — no. (%)** | | |
| 0 | 55 (70.5%) | 65 (83.3%) |
| 1 | 21 (26.9%) | 13 (16.7%) |
| **Race — no. (%)** | | |
| White | 75 (96.2%) | 76 (97.4%) |
| Asian | 1 (1.3%) | 1 (1.3%) |
| Black or African American | 0 | 0 |
| Not Reported | 2 (2.6%) | 1 (1.3%) |
| **Region — no. (%)** | | |
| United States of America | 29 (37.18%) | 34 (43.59%) |
| Belgium | 17 (21.79%) | 11 (14.10%) |
| United Kingdom | 21 (26.92%) | 17 (21.79%) |
| Norway | 11 (14.10%) | 16 (20.51%) |
| **Stage of disease at screening — no. (%)** | | |
| Stage IIIB | 2 ( 2.56%) | 2 ( 2.56%) |
| Stage IIIC | 4 ( 5.13%) | 9 (11.54%) |
| Stage IIID | 5 ( 6.41%) | 1 ( 1.28%) |
| Stage IV | 67 (85.90%) | 66 (84.62%) |
| **Metastasis stage — no. (%)** | | |
| M1a | 14 (17.95%) | 10 (12.82%) |
| M1b | 20 (25.64%) | 14 (17.95%) |
| M1c | 31 (39.74%) | 41 (52.56%) |
| M1d | 2 ( 2.56%) | 1 ( 1.28%) |
| Unknown | 0 | 0 |
| **Baseline LDH — no. (%)** | | |
| ≤ ULN | 50 (64.10%) | 46 (58.97%) |
| > ULN | 28 (35.90%) | 31 (39.74%) |
| > 2 x ULN | 5 ( 6.41%) | 16 (20.51%) |
| **BRAF mutation status — no. (%)** | | |
| Positive | 30 (38.46%) | 36 (46.15%) |
| Negative | 47 (60.26%) | 38 (48.72%) |
| Unknown | 1 ( 1.28%) | 4 ( 5.13%) |
| **Prior systemic therapy intent – no. (%)** | | |
| Neoadjuvant | 0 | 0 |
| Adjuvant | 10 (12.82%) | 12 (15.38%) |

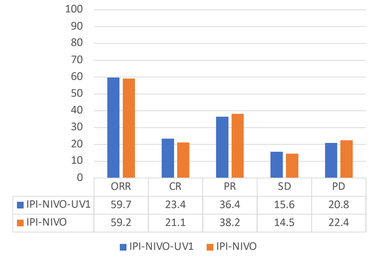
### Progression-free Survival




### Overall Survival




### Objective Response Rate

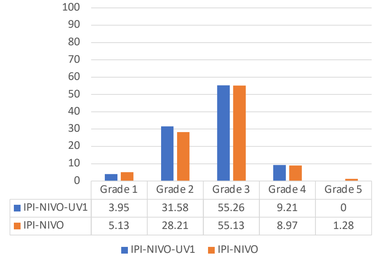


| | ORR | CR | PR | SD | PD |
|---|---|---|---|---|---|
| IPI-NIVO-UV1 | 59.7 | 23.4 | 36.4 | 15.6 | 20.8 |
| IPI-NIVO | 59.2 | 21.1 | 38.2 | 14.5 | 22.4 |

IPI-NIVO-UV1 IPI-NIVO

The ORR was similar with IPI-NIVO-UV1 and IPI-NIVO, at 60% vs 59%, respectively (Odds ratio 1.12, 95% CI 0.58-2.16, p value 0.867).

### Treatment Emergent AEs



| | Grade 1 | Grade 2 | Grade 3 | Grade 4 | Grade 5 |
|---|---|---|---|---|---|
| IPI-NIVO-UV1 | 3.95 | 31.58 | 55.26 | 9.21 | 0 |
| IPI-NIVO | 5.13 | 28.21 | 55.13 | 8.97 | 1.28 |

IPI-NIVO-UV1 IPI-NIVO

## CONCLUSION

UV1 did not improve on outcomes of IPI-NIVO, in terms of PFS. Longer follow-up is required for the accurate assessment of OS. No significant toxicity increases were observed with the addition of UV1. Data from a biomarker driven cohort are awaited.

## ACKNOWLEDGEMENTS

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