BERLIN 2025 ESMO congress

## LBA58

# PLUME: A single-arm phase II trial of pembrolizumab (pembro) plus lenvatinib (lenva) in patients (pts) with metastatic uveal melanoma (mUM)

M.J. Rodrigues[1], V. Servois[2], R. Sanchez[1], E. Bastien[3], E. Lafitte[3], C. Vacheret[3], Z. Castel Ajgal[3], M.P. Sablin[3], T. Ramtohul[2], S. Dureau[4], A. Savignoni[4], S. Piperno-Neumann[1]

[1] Medical Oncology Department, Institut Curie, Paris, France, [2] Radiology Department, Institut Curie, Paris, France, [3] Department of Drug Development and Innovation (D3i), Institut Curie, Paris, France[4] Biometry, Institut Curie, Paris, France

## Background

UM metastases are associated with poor prognosis. Tebentafusp (Tebe), a bispecific T-cell engager, benefits only HLA A*02-01+ mUM pts. Response to immune checkpoint inhibitors (ICI) is low. Lenva+pembro may enhance the antitumor immune response in mUM pts.

## Methods

Fifty-one ICI-naïve mUM pts were enrolled between July 2022 and October 2024 in PLUME, a monocentric, single-arm phase II trial at Institut Curie, Paris, France (NCT05282901). Two cohorts were assessed: HLA A*02-01neg, Tebe-naive pts (C1, n=22), and HLA A*02-01pos pts, pretreated with Tebe (C2, n=29). Pts received pembro (200 mg q3w, 35 cycles maximum) plus lenva (20mg QD until progression) and had liver MRI and chest-abdomen-pelvis CT every 9 weeks until progression. Primary endpoint was progression-free survival (PFS) at 27+/-2 weeks of treatment per RECIST v1.1 in each cohort. Secondary objectives included PFS according to iRECIST, overall survival, response rate, safety, and quality of life. Results were analyzed using one-stage Fleming design : if ≤16 (C1) or ≤17 (C2) failures occur over 27 weeks, the treatment was deemed effective in the cohort.

## Results

All patients were followed for more than 27 weeks. At 27 weeks, 15 progressions were observed in C1 corresponding to a 27-week PFS of 31.8% (95% confidence interval [CI] 13.9 – 54.9). C2 had 11 progressions with a 27-week PFS of 60.7% [40.6 - 78.5]. Safety was consistent with prior pembro/lenva trials and manageable. Lenva was held in 39 pts (76%), dose reduced in 13 (26%) and permanently discontinued in 2 (4%) for toxicity. Pembro was held in 11 pts (22%), and permanently discontinued in 2 (4%) for toxicity. No treatment-related deaths occurred.Table: LBA58

| | Cohort 1Tebentafusp-naive HLA A*02-01neg n=22 assessable pts | Cohort 2Tebentafusp-pretreated HLA A*02-01pos n=29 assessable pts |
|---|---|---|
| Predefined statistical threshold for success | ≤16 | ≤17 |
| Observed progressions at 27 weeks | 15 | 11 |
| % PFS at 27 weeks [IC95%] | 31.8% [13.9 - 54.9] | 60.7% [40.6 - 78.5] |

## Conclusions

Pembro+lenva met the predefined 27-week PFS success criteria in both Tebe-naïve and Tebe-pretreated cohorts, with particularly encouraging activity in Tebe-pretreated patients. Biomarker and real-world comparisons are ongoing.

## Clinical trial identification

NCT05282901.

## Legal entity responsible for the study

Institut Curie.

## Funding

Institut National du Cancer (INCa) PHRC-K 2020 and Merck Sharp & Dohme LLC.

## Disclosure

M.J. Rodrigues: Financial Interests, Personal, Invited Speaker: Immunocore; Financial Interests, Personal, Advisory Board: GSK, AstraZeneca; Financial Interests, Institutional, Coordinating PI: Johnson & Johnson, Daiichi Sankyo; Financial Interests, Institutional, Local PI: MSD; Non-Financial Interests, Institutional, Product Samples, For a phase 2 trial: MSD. Z. Castel Ajgal: Financial Interests, Personal, Advisory Board: Janssen; Financial Interests, Personal, Other, Conference support: Janssen, Bayer, Novartis. S. Piperno-Neumann: Financial Interests, Personal, Advisory Board: Immunocore, Pierre Fabre, Replimune, Deciphera. All other authors have declared no conflicts of interest.