Background NOUS-PEV is a vector-based personalized cancer vaccine, expressing about 60 patient-specific neoantigens identified by next-generation sequencing (NGS). Vaccination consists of Great Ape Adenoviral (GAd) prime followed by Modified Vaccinia Ankara (MVA) boosts. The study is a dose-confirmation and cohort expansion, phase 1b, first in human (FIH) trial (NCT04990479) evaluating safety, tolerability, immunogenicity and preliminary anti-tumour activity of NOUS-PEV in combination with the PD-1 blocking antibody pembrolizumab.

Methods The study is enrolling treatment-naive subjects with unresectable stage III/IV cutaneous melanoma and/or PD ligand 1 (PD-L1)/C2150% stage IV non-small cell lung cancer. Following pembrolizumab induction treatment (3 cycles), the vaccines are administered intramuscularly: the GAd priming dose concomitantly with pembrolizumab at week 10 (4th pembrolizumab infusion) followed by 3 boosts of MVA, each 3 weeks apart. Baseline and on-treatment tumor biopsies are collected at screening and post 1st MVA, respectively. PBMC are collected at baseline, post pembrolizumab, and post each vaccination for evaluation of immune response. Clinical response is evaluated according to RECIST v1.1 by CT scan according to standard of care.

Results All vaccines were made and administered on time to the three melanoma subjects in the dose-confirmation cohort. As of June 2022, the median follow-up is 6.9 months (range 3.0-11.5). No dose-limiting toxicities (DLTs) were observed, and the treatment was safe and no NOUS-PEV related AEs >Grade 1 were observed, allowing the enrollment of subjects in the expansion cohort.

In the first subject, the first CT scan before vaccination showed initial SD with dynamic of growth in target lesion size, that then reverted after NOUS-PEV administration, resulting in a confirmed PR deepening over time. The second subject had a PR already at the first CT scan, further deepened after the vaccination. The third subject had PD at the first scan before vaccination and discontinued based on the confirmatory scan.

Vaccine-induced immunogenicity was demonstrated by ex vivo interferon-gamma ELISpot in 2 evaluable subjects who showed clinical response, with detection of potent neoantigen specific immune response to multiple neoantigens in the peripheral blood and induction of both CD4 and CD8 T cell responses. NGS analysis of baseline and on-treatment biopsies showed an increased T cell infiltrate, with expansion and diversification of the TCR repertoire post treatment.

Conclusions NOUS-PEV in combination with anti-PD1 is safe and well tolerated. Data show that vaccination elicits a robust immune response which correlates with preliminary clinical activity.

Trial Registration NCT04990479

Ethics Approval The study was approved by UZ Leuven Ethics Committee (Study Reference S64578) and by Research Ethics Committee of Fundacion Jimenez Diaz, Madrid