Updated survival and vaccine response from the NIPU trial; A randomised, phase II study evaluating nivolumab and ipilimumab with or without UV1 vaccination in patients with pleural mesothelioma

Background

While immunotherapy has improved survival for some patients with pleural mesothelioma (PM), prognosis is still dismal with poor immune response for many patients. The NIPU trial evaluated adding UV1 telomerase vaccine to immunotherapy. The first survival data presented at ESMO 2023 did not meet the primary end-point of improved progression-free survival (PFS) by blinded, independent central review (BICR). Here we present updated survival and analysis of UV1-specific immune response.

Methods

Patients with PM progressing after first-line platinum-based chemotherapy were randomized 1:1 to ipilimumab and nivolumab alone (Arm B) or in combination with the telomerase vaccine UV1 (Arm A). Peripheral blood mononuclear cells (PBMC) were collected from a subset of patients. The cells were cultured and stimulated with UV1 peptides to identify patients with UV1-specific immune reaction.

Results

118 patients were randomized. With a median follow-up of 24.9 months (95% CI 21,8-31,3), investigator determined PFS events has occurred for 107 patients (91%) and OS events for 86 (73%).

Investigator-determined PFS was not significantly different between treatment arms for all patients (hazard ratio (HR) 0.77 80% CI 0.59-1.0, p=0.197), but for the epithelioid subgroup (Cox HR 0.64, p=0.047) with median PFS 5.5 months in the UV1 arm, (95% CI 3.8-9.7) vs 2.9 in arm B (95% CI 2.1-6.2), p=0.044. For OS, the HR was 0.81 (80% CI 0.61-1.08, p=0.345). Successful proliferation of PBMC enabling analysis was achieved for 10 pts in arm A and 13 in arm B analysed at baseline and 6 and 12 weeks after randomisation. Of the evaluable patients, 4 developed UV1 specific response in arm A and none in arm B. 3/4 patients with UV1-specific response and 2/6 without had partial response or stable disease at the same time-points.

Conclusion

There is no significant difference in OS between the treatment arms. UV1-specific response is detected in some patients receiving UV1 vaccine, and will be further explored. Translational analyses will investigate whether some patients with epithelioid histology benefit more from UV1, warranting further clinical studies.