Real-world evidence of the impact of immunotherapy (IT) on overall survival (OS) of patients (p) with malignant pleural mesothelioma (MPM) adjusted for tumor histology

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Background
In 1st-line setting in MPM CheckMate-743 trial demonstrated better outcomes for IT over chemotherapy in p with no-epithelioid histology. However, another trials (MAPS2, DREAM) demonstrated efficacy of IT in all tumors. The objective of this study is to characterize the impact of IT according to histology in p with MPM.

Methods
Clinical records of MPM p treated with IT (anti-PD1/L1) at Vall d’Hebron University Hospital were reviewed. Associations between clinical variables and outcome were assessed with multivariate time-dependent Cox regression models to adjust for immortal-time bias and histology. Survival data were calculated by the Kaplan-Meier method.

Results
228 p were reviewed: median age 68 years (29-88), males: 70%, performance status (PS): 69%, epithelioid: 82%. Median overall survival (OS) of the entire cohort was 21.4 months (m) (CI95% 18-23.8). Epithelioid histology, PS 0, stage 1-2 and treatment with cisplatin were associated with significant improvements in OS (p<0.001). Thirty-six p (16%) were treated with anti-PD1/L1 (13 p in 1st line, 23 p in 2nd or further lines). In the multivariable time-dependent model, both histology (HR=0.51) and exposure to IT (HR=0.66) had significant impact on OS (P-values <0.1). Patients with epithelioid tumors treated with anti-PD1/L1 at any line had a median OS of 33.1 m (vs 23.8 m for p without IT), while p with non-epithelioid tumors exposed to anti-PD1/L1 had median OS of 19.5 m (vs 14.1 m without IT). In p exposed to IT in 2nd or further lines, median OS for p with epithelioid tumors treated with IT was 24.2 m (vs 13.7 m in p without IT), and for non-epithelioid cases median OS was 6.6 m and 10.0 m for p treated with or without IT respectively.

Conclusions
In our series of real-word MPM treated with IT we did demonstrate a benefit of IT for MPM p. Considering the prognostic effect of histology and the potential immortal time bias for IT exposure, we demonstrated improved OS for p receiving IT with a trend of higher benefit in epithelioid tumors. Ongoing studies combining checkpoint inhibitors plus chemotherapy are evaluating the impact of histology in the outcomes.

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