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First-line nivolumab (NIVO) plus ipilimumab (IPI) vs chemotherapy (chemo) in patients (pts) with unresectable malignant pleural mesothelioma (uMPM): 4-year update from CheckMate 743

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Background

In the randomized, phase 3 CheckMate 743 study (NCT02899299), NIVO + IPI significantly prolonged OS vs chemo in pts with uMPM. Identifying pts with uMPM who could benefit from immunotherapy is an unmet need. Here, we report clinical results and exploratory biomarker analyses from CheckMate 743 at 4y minimum follow-up (min f/u).

Methods

Pts with previously untreated uMPM, stratified by histology and sex, were randomized 1:1 to receive NIVO (3 mg/kg Q2W) + IPI (1 mg/kg Q6W) for up to 2 y, or chemo (Q3W) for ≤ 6 cycles. Primary endpoint (EP) was OS; secondary EPs included PFS and ORR; exploratory EPs were safety and biomarker analyses. OS was assessed by baseline (BL) soluble mesothelin (sMESO) levels (high, mid, low by ELISA-based assay) and MPM-specific tumor suppressor mutations (*TP53, BAP1, SETD2, NF2, LATS2* using whole-exome sequencing).

Results

At 47.5-month min f/u (database lock [DBL] 6 May 2022), NIVO + IPI continued to show OS benefit vs chemo with 4y OS rates of 16.8% vs 10.7%; 4y PFS rates were 9.0% vs 0%, respectively (Table). High (vs low or mid) BL sMESO level was associated with shorter OS in both arms; NIVO + IPI showed a trend of improved OS vs chemo across BL sMESO levels (HRs [95% CI], high: 0.72 [0.53–0.98], mid: 0.77 [0.56–1.06], low: 0.77 [0.56–1.05], respectively). OS favored NIVO + IPI vs chemo for both wild-type (HRs = 0.67–0.72) and MPM-specific tumor suppressor mutation subgroups (HRs = 0.41–0.55), except *SETD2* mutation (HR = 1.37). Consistent with the prior DBL, the most common grade 3/4 immune-mediated adverse events with NIVO + IPI were hepatitis (5%), diarrhea/colitis (4%), and rash (3%).Table: LBA71

Efficacy outcomes with NIVO + IPI vs chemo

	NIVO + IPI (n = 303)	Chemo (n = 302)
OSMedian (95% CI), moHR (95% CI) vs chemo4y OS rate (95% CI), %	18.1 (16.8–21.0)0.73 (0.61–0.87)16.8 (12.7–21.5)	14.1 (12.4–16.3)-10.7 (7.5–14.7)
4y PFS[a]rate (95% CI), %	9.0 (5.2–14.1)	– [c]
ORR[a] (95% CI), %	39.3 (33.7–45.0)	44.4 (38.7–50.2)
Median DOR[a,b] (95% CI), mo	11.6 (8.2–16.8)	6.8 (5.6–7.1)

[a]Per blinded independent central review;[b]Calculated in patients with a response (NIVO + IPI, n = 119; chemo, n = 134);[c]All pts either had

disease progression or were censored by month 39. DOR, duration of response; ORR, objective response rate; OS, overall survival; PFS, progression-free survival.

Conclusions

With 4y min f/u, NIVO + IPI continued to provide long-term, durable OS benefit vs chemo in pts with uMPM. No new safety signals were seen. High BL sMESO levels were prognostic for poor OS. OS benefit with NIVO + IPI vs chemo was generally observed regardless of MPM-specific tumor suppressor mutations.

Clinical trial identification

NCT02899299.

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Legal entity responsible for the study

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Disclosure

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