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LBA65

First-line nivolumab (NIVO) plus ipilimumab (IPI) vs chemotherapy (chemo) in patients (pts) with unresectable malignant pleural mesothelioma (MPM): 3-year update from CheckMate 743

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Background

In the randomized phase 3 CheckMate 743 study (NCT02899299), NIVO + IPI significantly prolonged overall survival (OS) vs chemo in pts with unresectable MPM. Here we report updated efficacy and safety with a 3-y minimum follow-up (f/u), as well as novel biomarker analyses.

Methods

Pts with untreated MPM, stratified by histology (epithelioid vs non-epithelioid) and sex, were randomized 1:1 to NIVO 3 mg/kg Q2W + IPI 1 mg/kg Q6W (≤ 2 y) or to chemo Q3W (6 cycles). The primary endpoint was OS; safety and biomarker assessments were prespecified exploratory endpoints. OS association with a 4-gene inflammatory gene expression signature (*CD8A, PD-L1, STAT-1, LAG-3*) was estimated by RNA sequencing and categorized as high vs low relative to median score. Lung immune prognostic index (LIPI) score was based on baseline (BL) derived neutrophil-to-lymphocyte ratio and lactate dehydrogenase levels.

Results

With a minimum f/u of 35.5 mo (database lock [DBL] 7 May 2021), NIVO + IPI continued to provide OS benefit vs chemo (HR 0.75, 95% CI 0.63–0.90; Table). In exploratory biomarker analyses, median OS was longer for pts with high vs low inflammatory gene signature score (21.8 vs 16.8 mo) in the NIVO + IPI arm; this signature score was not associated with prolonged OS for chemo. OS showed a trend favoring NIVO + IPI vs chemo across good, intermediate, and poor BL LIPI subgroups; HR (95% CI), 0.78 (0.60–1.01), 0.76 (0.57–1.01), and 0.83 (0.44–1.57), respectively. Grade 3–4 treatment-related adverse events occurred in 30.7% (NIVO + IPI) and 32.0% (chemo) of pts; no increase was reported from the previous DBL.Table: LBA65

Efficacy outcomes with NIVO + IPI vs chemo

	NIVO + IPI (n = 303)	Chemo (n = 302)
OS		
Median (95% CI), mo	18.1 (16.8–21.0)	14.1 (12.4–16.3)
HR vs chemo (95% CI)	0.75 (0.63–0.90)	—
3-y OS rate (95% CI), %	23.2 (18.4–28.2)	15.4 (11.5–19.9)
3-y PFS[a] rate (95% CI), %	13.6 (9.4–18.6)	0.8 (0.1–3.9)
ORR[a] (95% CI), %	39.6 (34.1–45.4)	44.0 (38.4–49.8)

	NIVO + IPI (n = 303)	Chemo (n = 302)
DOR[a,b]		
Median (95% CI), mo	11.6 (8.2–16.8)	6.7 (5.6–7.1)
3-y DOR rate, %	28	0

[a]Per blinded independent central review; [b]Calculated in patients with a response (NIVO + IPI, n = 120; chemo, n = 133). DOR, duration of response; ORR, objective response rate; PFS, progression-free survival.

Conclusions

With a 3-y minimum f/u, NIVO + IPI continued to provide survival benefit vs chemo in pts with unresectable MPM despite pts being off therapy for 1 y; no new safety signals were observed. Exploratory analyses suggest that a high inflammatory gene signature score may correlate with improved survival benefit with NIVO + IPI.

Clinical trial identification

NCT02899299; 14 September 2016.

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Legal entity responsible for the study

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