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CheckMate 204: 3-year outcomes of treatment with combination nivolumab (NIVO) plus ipilimumab (IPI) for patients (pts) with active melanoma brain metastases (MBM)

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Background

In CheckMate 204, asymptomatic pts (cohort A) with active, untreated MBM achieved high intracranial (IC) and extracranial (EC) response rates with NIVO + IPI; efficacy was lower in pts with symptomatic and/or steroid-requiring MBM (cohort B). Here, we report 3-y response and survival outcomes in both cohorts, along with first results of the blinded independent central review (BICR) of imaging data.

Methods

In this open-label, multicenter, phase II study, pts with metastatic melanoma and ≥ 1 nonirradiated brain metastasis 0.5–3 cm in diameter received NIVO 1 mg/kg + IPI 3 mg/kg Q3W × 4, followed by NIVO 3 mg/kg Q2W until progression or unacceptable toxicity. The primary endpoint was IC clinical benefit rate, defined as the proportion of pts with complete response (CR), partial response (PR), or stable disease (SD) ≥ 6 mo (per modified RECIST 1.1). Investigator (INV)-assessed and BICR-assessed response and PFS were evaluated along with OS.

Results

At an overall minimum follow-up of 34 mo (median follow-up: 34 mo, cohort A; 7.5 mo, cohort B), there were 101 INV-assessed asymptomatic pts (95 BICR-evaluable) and 18 symptomatic pts (17 BICR-evaluable). INV- and BICR-response rates were consistent (table), with a concordance rate among evaluable pts of 85% for cohort A and 94% for cohort B. For cohort A, 36-mo IC progression-free survival (PFS) was 54% (95% CI, 43–64) by INV and 52% (41–62) by BICR, and overall survival (OS) was 72% (62–80). For cohort B, 36-mo IC PFS was 19% (95% CI, 5–40) by INV and 28% (10–50) by BICR, and OS was 37% (14–60). No new safety signals or treatment-related deaths were reported.

Conclusions

High concordance was observed between INV- and BICR-assessed responses in this trial for both cohorts. The durable 3-y OS and PFS rates for the asymptomatic cohort support the use of first-line NIVO + IPI. Symptomatic pts with MBM remain difficult to treat, but some can derive long-term benefit from NIVO + IPI.Table: 1039MO

	INV			BICR		
	IC	EC	Global	IC	EC	Global
Asymptomatic, n (%)	N = 101	N = 101[a]				

	INV			BICR		
	IC	EC	Global	IC	EC	Global
CR	33 (33)	16 (16)	17 (17)	26 (26)	14 (14)	11 (11)
PR	21 (21)	33 (33)	35 (35)	24 (24)	36 (36)	38 (38)
SD ≥ 6 mo	4 (4)	5 (5)	4 (4)	4 (4)	5 (5)	3 (3)
ORR, n (%; 95% CI)	54 (54; 43–64)	49 (49; 38–59)	52 (51; 41–62)	50 (50; 39–60)	50 (50; 39–60)	49 (49; 38–59)
Symptomatic, n (%)	N = 18	N = 18[a]				
CR	3 (17)	1 (6)	1 (6)	3 (17)	2 (11)	2 (11)
PR	0	3 (17)	3 (17)	1 (6)	2 (11)	2 (11)
SD ≥ 6 mo	0	0	0	0	0	0
ORR, n (%; 95% CI)	3 (17; 4–41)	4 (22; 6–48)	4 (22; 6–48)	4 (22; 6–48)	4 (22; 6–48)	4 (22; 6–48)

[a]Total patients includes 6 asymptomatic pts and 1 symptomatic pt for whom BICR data were not available. CI, confidence interval; ORR, objective response rate.

Clinical trial identification

NCT02320058.

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Legal entity responsible for the study

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