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Nivolumab plus ipilimumab (NIVO + IPI) vs lenvatinib or sorafenib (LEN/SOR) as first-line (1L) treatment for unresectable hepatocellular carcinoma (uHCC): Efficacy in patients (pts) with poor prognosis and hepatic safety in the overall population from CheckMate 9DW

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Background

In the phase 3 CheckMate 9DW trial, at 35.2-month (mo) median follow-up, 1L NIVO + IPI showed significant overall survival (OS) benefit vs LEN/SOR (HR, 0.79 [95% CI, 0.65–0.96]; $P = 0.018$), higher objective response rate (ORR; 36% vs 13%; $P < 0.0001$) by blinded independent central review, and manageable safety in pts with uHCC. We present subgroup efficacy in pts with uHCC with poor prognostic factors at baseline and hepatic safety analyses from this follow-up.

Methods

Adults with uHCC without prior systemic therapy were randomized to NIVO 1 mg/kg + IPI 3 mg/kg Q3W (up to 4 cycles) followed by NIVO 480 mg Q4W or investigator's choice of LEN 8 mg or 12 mg QD or SOR 400 mg BID (Yau T et al. *Lancet*, ePub 2025). Pts with poor prognosis were defined as those with baseline characteristics such as Barcelona Clinic Liver Cancer (BCLC) stage C, alpha-fetoprotein (AFP) ≥ 400 ng/ml, macrovascular invasion (MVI), or ECOG performance status (PS) 1.

Results

Pts were randomized to NIVO + IPI (n = 335) or LEN/SOR (n = 333). Consistent with findings in the overall population, OS favored NIVO + IPI over LEN/SOR in pts with poor prognostic factors at baseline (Table). Additional OS and ORR subgroup analyses will be presented. Among 332 pts treated with NIVO + IPI, any-grade hepatic immune-mediated adverse events (IMAEs) occurred in 63 (19%) pts, of which 51 (15%) had grade 3/4 events and 56 (17%) received high-dose steroids. Hepatic IMAEs led to treatment discontinuations in 19 (6%) pts.Table: 1486P

	NIVO + IPI mOS (95% CI), mo	LEN/SOR	HR (95% CI)
Overall (N = 668)	23.7 (18.8–29.4)	20.6 (17.5–22.5)	0.79 (0.65–0.96)
MVI-Yes (n = 169)	22.9 (15.2–NE)	15.4 (10.3–20.1)	0.59 (0.40–0.87)
BCLC C (n = 488)	20.3 (16.9–25.8)	17.8 (15.5–21.1)	0.81 (0.65–1.01)
ECOG PS 1 (n = 191)	16.4 (10.0–23.0)	15.3 (10.3–17.4)	0.78 (0.55–1.09)
AFP ≥ 400 ng/ml (n = 221)	16.4 (10.3–25.5)	12.1 (8.7–16.3)	0.69 (0.50–0.95)

NE, not estimable.

Conclusions

OS consistently favored 1L NIVO + IPI over LEN/SOR in subgroups of pts with uHCC who had certain poor prognostic factors at baseline. Hepatic IMAEs were manageable with established algorithms and most did not lead to discontinuation. These results furthersupport1L NIVO +IPIas a standard of care in uHCC.

Clinical trial identification

NCT04039607.

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Disclosure

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