Nivolumab (NIVO) plus ipilimumab (IPI) vs lenvatinib (LEN) or sorafenib (SOR) as first-line (1L) therapy for unresectable hepatocellular carcinoma (uHCC): CheckMate 9DW expanded analyses.

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Background: In the phase 3 CheckMate 9DW study (NCT04039607), 1L NIVO + IPI demonstrated significant overall survival (OS) benefit vs LEN/SOR, higher objective response rate (ORR) with durable responses, and manageable safety in uHCC. We present efficacy by best overall response (BOR) subgroups and baseline characteristics, and additional safety analyses from the preplanned interim analysis. **Methods:** Patients (pts) with previously untreated HCC not eligible for curative surgical or locoregional therapies, Child-Pugh score 5 or 6, and ECOG performance status 0 or 1 were randomized 1:1 to receive NIVO 1 mg/kg + IPI 3 mg/kg Q3W (up to 4 cycles), then NIVO 480 mg Q4W or LEN 8 mg or 12 mg QD or SOR 400 mg BID until disease progression or unacceptable toxicity. NIVO was given for a maximum of 2 years. The primary endpoint was OS; secondary endpoints included ORR and duration of response (DOR) per blinded independent central review (BICR) using RECIST v1.1. **Results:** A total of 668 pts were randomized to NIVO + IPI (n = 335) or LEN/SOR (n = 333). At a median follow-up of 35.2 (range 26.8–48.9) months (mo), median OS (95% CI) was 23.7 (18.8–29.4) mo with NIVO + IPI vs 20.6 (17.5–22.5) mo with LEN/SOR (HR 0.79 [95% CI 0.65–0.96]; $P = 0.0180$). ORR (95% CI) per BICR was significantly higher with NIVO + IPI vs LEN/SOR (36% [31–42] vs 13% [10–17]; $P < 0.0001$); median DOR (95% CI) was 30.4 (21.2–not estimable [NE]) mo vs 12.9 (10.2–31.2) mo. Survival benefit of NIVO + IPI vs LEN/SOR was observed across BOR subgroups at the 24-week landmark timepoint (Table). In subgroup analyses, ORR (95% CI) per BICR was higher with NIVO + IPI vs LEN/SOR across HCC etiologies (uninfected: 35% [26–44] vs 8% [4–15]; HBV infected: 25% [17–34] vs 17% [10–25]; HCV infected: 50% [39–61] vs 16% [9–25]) and in pts with Barcelona Clinic Liver Cancer stage ≤B (33% [23–43] vs 13% [6–21]) or stage C (37% [31–44] vs 14% [10–19]). Safety data are shown in the Table. Additional exploratory analyses will be presented. **Conclusions:** These additional analyses from CheckMate 9DW demonstrate the efficacy and manageable safety of 1L NIVO + IPI in uHCC and further support its use as a potential standard-of-care treatment option in this setting. Clinical trial information: NCT04039607. Research Sponsor: Bristol Myers Squibb.

OS by BOR at week 24 landmark	NIVO + IPI			LEN/SOR		
BOR	CR + PR (n = 101)	SD[a] (n = 105)	PD (n = 47)	CR + PR (n = 28)	SD[a] (n = 212)	PD (n = 31)
Median OS (95% CI), mo	NR (44.4–NE)	30.0 (23.5–37.8)	16.0 (12.0–18.7)	28.3 (20.6–NE)	22.5 (20.5–24.8)	13.5 (8.7–25.3)
All treated pts	**NIVO + IPI (n = 332)**			**LEN/SOR (n = 325)**		
Any-grade/grade 3–4 TRAEs, n (%)	278 (84)/137 (41)			297 (91)/138 (42)		
Hepatobiliary	44 (13)/35 (11)			15 (5)/10 (3)		
Cardiovascular	10 (3)/3 (< 1)			138 (42)/39 (12)		
Hemorrhagic	2 (< 1)/1 (< 1)			20 (6)/5 (2)		

[a]Includes non-CR/non-PD. CR, complete response; NR, not reached; PD, progressive disease; PR, partial response; SD, stable disease; TRAE, treatment-related adverse event.