LBA18_PR

Durable clinical benefit with nivolumab (NIVO) plus low-dose ipilimumab (IPI) as first-line therapy in microsatellite instability-high/mismatch repair deficient (MSI-H/dMMR) metastatic colorectal cancer (mCRC)

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Background: In previously chemotherapy-treated patients with MSI-H/dMMR mCRC from the phase II CheckMate-142 trial, NIVO + low-dose IPI (1 mg/kg) provided durable clinical benefit (investigator-assessed [INV] objective response rate [ORR] 55%, median duration of response [DOR] not reached, 12-month overall survival [OS] rate 85%) and manageable safety. Here we report the first results of the efficacy and safety of NIVO + low-dose IPI as a first-line (1L) therapy for patients with MSI-H/dMMR mCRC from CheckMate-142.

Methods: Patients with no prior treatment for MSI-H/dMMR mCRC were treated with NIVO 3 mg/kg every 2 weeks (Q2W) + low-dose IPI every 6 weeks (Q6W) until disease progression. The primary endpoint was ORR (INV; RECIST v1.1).

Results: Of 45 patients, 51% were male and median age was 66 years. Median follow-up (time from first dose to data cut-off) was 13.8 months (range 9–19). The ORR and disease control rate (DCR) were 60% and 84%, respectively, with a 7% complete response rate (Table). Median DOR was not reached. At 12 months, progression-free survival (PFS) and OS rates were 77% and 83%, respectively. Grade 3–4 treatment-related adverse events (TRAEs) occurred in 16% of patients and 7% of patients had any grade TRAEs leading to discontinuation. Any grade select immune-mediated TRAEs affecting the hepatic (13%), gastrointestinal (11%), pulmonary (2%), and renal (2%) systems resolved in 100% of patients, while those affecting the skin (33%) and endocrine (24%) systems resolved in 45% and 60% of patients, respectively.

Conclusions: NIVO (Q2W) + low-dose IPI (Q6W) demonstrated robust and durable clinical benefit and was well-tolerated as a 1L treatment for MSI-H/dMMR mCRC. These results suggest that NIVO + low-dose IPI may represent a new treatment option for these patients.

Clinical trial identification: NCT02060188.

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Table: LBA18_PR Efficacy and safety

	NIVO + IPI (N = 45)
ORR[a], n (%) (95% CI)	27 (60) (44–74)
Best overall response, n (%) CR PR SD PD Not determined	3 (7) 24 (53) 11 (24) 6 (13) 1 (2)
DCR[b], n (%) (95% CI)	38 (84) (71–94)
Median time to response, months (range)	2.6 (1.2–13.8)
Median DOR, months (95% CI)	NR (11.5–NE)
Median PFS, months (95% CI) 12-month rate, % (95% CI)	NR (14.1–NE) 77 (62.0–87.2)
Median OS, months (95% CI) 12-month rate, % (95% CI)	NR (NE) 83 (67.6–91.7)
TRAEs, n (%) Any grade Grade 3–4	35 (78) 7 (16)
TRAEs leading to discontinuation, n (%) Any grade Grade 3–4	3 (7) 1 (2)

[a]Patients with CR or PR divided by the number of treated patients

[b]Patients with a CR, PR, or SD for ≥12 weeks divided by the number of treated patients CI = confidence interval; CR = complete response; NE = not estimable; NR = not reached; PD = progressive disease; PR = partial response; SD = stable disease