SO-27 Nivolumab plus low-dose ipilimumab in previously treated patients with microsatellite instability-high/mismatch repair-deficient metastatic colorectal cancer: 4-year follow-up from CheckMate 142

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Background: In the phase 2 multicohort CheckMate 142 study (NCT02060188), nivolumab plus low-dose (1 mg/kg) ipilimumab provided robust and durable clinical benefit with a manageable safety profile in previously treated patients with microsatellite instability-high/mismatch repair-deficient (MSI-H/dMMR) metastatic colorectal cancer (mCRC) at a median follow-up of 13.4 months (Overman M et al. J Clin Oncol 2018;36:773—779). At 25.4 months of follow-up, nivolumab plus low-dose ipilimumab continued to provide robust and durable clinical benefit with deepening of response, and no new safety signals were identified (Overman M et al. J Clin Oncol 2019;37:635). Here, we present results from the 4-year follow-up of these patients.

Methods: Patients received nivolumab (3 mg/kg) + low-dose (1 mg/kg) ipilimumab Q3W (4 doses) followed by nivolumab (3 mg/kg) Q2W until disease progression. Primary endpoint was investigator-assessed objective response rate (ORR; per RECIST v1.1). Other key endpoints reported here include disease control rate (DCR, per investigator), duration of response (DOR, per investigator), progression-free survival (PFS, per investigator), overall survival (OS), and safety.

Results: For the 119 treated patients, median age was 58 years, 59% were male, 76% had $\geq$ 2 prior lines of therapy, 55% had ECOG performance status (PS) 1, 25% had BRAF mutation, 37% had KRAS mutation, and 26% were BRAF/KRAS wild type. Median follow-up was 50.9 months (range, 46.9—62.7 months). Investigator-assessed ORR (95% CI) increased from 55% (45—64) at 13.4 months to 65% (55—73) at 50.9 months; DCR (95% CI) at 50.9 months was 81% (72—87). Complete response (CR) rate increased with longer follow-up from 3% at 13.4 months to 13% at 50.9 months. Partial responses (PR) were observed in 52% of patients; 21% had stable disease (SD), and 12% had progressive disease (PD) as best response. Median time to response was 2.8 months (range, 1.1—37.1 months) and median DOR was not reached (range, 1.4+ to 58.0+ months). At data cutoff, 37 (48%) patients had ongoing responses. Median PFS was not reached (95% CI, 38.4 to not estimable [NE]) and median OS was not reached (95% CI, NE). The 48-month rates of PFS (95% CI) and OS (95% CI) were 53% (43—62) and 70.5% (61.4—77.9), respectively. ORR benefit was observed across evaluated subgroups by BRAF/KRAS mutation status, ECOG PS, age, and sex, and each was consistent with that in the overall population. Grade 3-4 treatment-related adverse events (TRAEs) were observed in 32% of patients; 10% (grade 3-4) and 13% (any grade) of patients had TRAEs leading to discontinuation.

Conclusions: Nivolumab plus low-dose ipilimumab provided durable clinical benefit (ORR, PFS, and OS) over 13.4, 25.4, and 50.9 months of follow-up. Extended follow-up

showed increasing ORR and deepening of response. The safety profile was manageable with no new safety signals. These results demonstrate long-term benefit of nivolumab plus low-dose ipilimumab for previously treated patients with MSI-H/dMMR mCRC.

Clinical trial identification: NCT02060188.

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