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Adjuvant nivolumab vs placebo for high-risk muscle-invasive urothelial carcinoma: 5-year efficacy and ctDNA results from CheckMate 274

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Background

The phase 3 CheckMate 274 trial of adjuvant nivolumab (NIVO) vs placebo (PBO) in patients (pts) with high-risk muscle-invasive urothelial carcinoma (MIUC) after radical surgery met the primary endpoints of improvement in disease-free survival (DFS) with NIVO vs PBO in intent-to-treat (ITT) pts and pts with tumor programmed death ligand 1 (PD-L1) expression ≥ 1%; efficacy improvements were continued at the 3-year follow-up. Interim overall survival (OS) also favored NIVO vs PBO. Here, we report extended 5-year follow-up results and exploratory circulating tumor (ct)DNA data.

Methods

Pts were randomized 1:1 to NIVO 240 mg IV every 2 weeks or PBO for ≤ 1 year of adjuvant treatment. Pts had radical surgery ± neoadjuvant chemotherapy and were at high risk of recurrence. Primary endpoints were DFS in ITT pts and pts with PD-L1 ≥ 1%. OS and disease-specific survival (DSS) were secondary endpoints. Analysis of ctDNA (with the Natera Signatera assay) was exploratory.

Results

A total of 709 pts (NIVO, n = 353; PBO, n = 356) were randomized. With median follow-up of 43.4 months, improvement in DFS was observed with NIVO vs PBO, and OS and DSS were longer with NIVO vs PBO, both in ITT and PD-L1 ≥ 1% pts (Table). No new safety signals were observed. 133/709 pts (18.8%) had evaluable cycle 1 day 1 ctDNA results; 54/133 (40.6%) pts were ctDNA positive(+). Improvement in DFS was observed with adjuvant NIVO vs PBO in pts with cycle 1 day 1 ctDNA(+), but not in pts with cycle 1 day 1 ctDNA(–).Table: 3068O

Outcome	Population	NIVO Mdn (95% CI), mo	PBO Mdn (95% CI), mo	HR (95% CI)
DFS	ITT	21.9 (18.8–36.9)	11.0 (8.3–16.6)	0.74 (0.61–0.90)
PD-L1 ≥ 1%	55.5 (25.8–66.5)	8.4 (5.6–20.0)	0.58 (0.42–0.79)	
ctDNA(+)[a]	7.4 (2.8–19.2)	2.8 (2.4–5.0)	0.35 (0.2–0.7)	
ctDNA(–)[a]	91.9 (19.2–NE)	52.2 (16.9–NE)	0.99 (0.5–1.9)	
OS[b]	ITT	75.0 (56.7–NE)	50.1 (38.0–72.1)	0.83 (0.67–1.02)
PD-L1 ≥ 1%	NR (70.0–NE)	59.4 (29.1–NE)	0.63 (0.44–0.90)	
DSS	ITT	NR (91.9–NE)	NR (52.1–NE)	0.79 (0.62–1.00)
PD-L1 ≥ 1%	NR (NE–NE)	92.1 (54.4–NE)	0.57 (0.37–0.87)	

[a]Exploratory analysis. [b]Follow-up is ongoing; prespecified statistical significance boundary not crossed at the time of analysis) Mdn

[a]Exploratory analysis. [b]Follow-up is ongoing, prespecified statistical significance boundary not crossed at the time of analysis).Mdn, median; NE, not estimable; NR, not reached.

Conclusions

With 5 years median follow-up, continued improvement in DFS with NIVO vs PBO was observed. OS and DSS were longer with NIVO vs PBO. Efficacy benefit was seen both in ITT and PD-L1 ≥ 1% pts. ctDNA analysis was consistent with prior observations of adjuvant immune checkpoint inhibitor blockade in MIUC. These long-term results support adjuvant NIVO as a standard of care in pts with high-risk MIUC.

Clinical trial identification

NCT02632409.

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Legal entity responsible for the study

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Disclosure

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