

2594MO Association of circulating kidney injury molecule-1 (KIM-1) levels with clinical outcomes in advanced renal cell carcinoma (aRCC): Retrospective analysis of COSMIC-313

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Background

KIM-1 levels have been associated with clinical outcomes in patients (pts) with aRCC treated with immuno-oncology (IO) and vascular endothelial growth factor receptor tyrosine kinase inhibitors (VEGFR TKI). Here, the relationship of KIM-1 levels with outcomes was assessed in the COSMIC-313 study (NCT03937219), which evaluated cabozantinib, nivolumab, and ipilimumab (C+N+I) vs N+I in first-line aRCC.

Methods

Pts were randomized to C+N+I or N+I (Choueiri et al. *N Engl JMed* 2023). Plasma KIM-1 was measured at baseline and 4 weeks after the first dose using an enzyme based electrochemiluminescence assay, and the association between KIM-1 levels and clinical outcomes evaluated. The KIM-1 longitudinal changes cutoff was identified using lowest *P* value approach.

Results

Paired baseline and week 4 KIM-1 levels were available for 635/855 (74%) pts. Median baseline KIM-1 levels were similar between arms. Higher baseline KIM-1 levels were associated with worse baseline IMDC risk, no prior nephrectomy, and increased tumor burden. In adjusted multivariate analysis, higher baseline KIM-1 was linked to shorter OS, but not PFS in both arms. Pts treated with C+N+I had a greater reduction in KIM-1 levels from baseline to week 4 vs N+I (90% vs 64%). An early decrease in KIM-1 levels was associated with improved ORR, PFS, and OS for N+I but not C+N+I (Table). KIM-1 kinetics differed after treatment with IO+IO vs IO+VEGFR TKI. Analysis of KIM-1 levels at weeks 7, 10, and 14 is ongoing and results will be presented.

Conclusions

High baseline KIM-1 levels were prognostic of worse clinical outcomes in COSMIC-313. Early reduction in KIM-1 levels from baseline to week 4 was associated with improved outcomes with N+I but not C+N+I, consistent with results from Checkmate-214 (Xu W et al. ASCO GU 2025). These data suggest that KIM-1 is prognostic for outcomes and an early biomarker of response to IO in aRCC.
Table: 2594MO

	C+N+I (n=314)		N+I (n=321)	
Change in KIM-1 levels ^a	Increase	Decrease	Increase	Decrease
n (%)	33 (10)	281 (90)	115 (36)	206 (64)
Median OS (95% CI), months	NE (36.1–NE)	41.9 (35.1–49.8)	26.9 (20.4–37.3)	53.1 (48.0–NE)
HR (95% CI); <i>P</i> value	1.3 (0.75–2.3); 0.35	0.5 (0.36–0.68); 0.000016		
Median PFS (95% CI), months	9.6 (5.2–NE)	22.3 (14.1–29.0)	5.8 (4.0–9.4)	19.4 (14.0–28.3)
HR (95% CI); <i>P</i> value	0.75 (0.48–1.2); 0.21	0.52 (0.39–0.69); 0.000011		
ORR (95% CI), %	43.8 (26.8–62.1)	49.0 (42.9–55.2)	24.7 (17.2–34.1)	48.7 (41.6–55.9)

^aFrom baseline to week 4. CI, confidence interval; HR, hazard ratio; NE, not estimable.

Clinical trial identification

NCT03937219.

Legal entity responsible for the study

Exelixis, Inc.

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Disclosure

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