Supplementary Material

Supplementary Tables

Table S1. *Patient Characteristics at Baseline.*

Baseline Characteristic	N=29
Age at treatment initiation (years), mean (SD)	73.4 (9.7)
Sex, n (%)	
Female	16 (55.2%)
Male	13 (44.8%)
Race, n (%)	
Caucasian	29 (100.0%)
Hypertension, n (%)	13 (44.8%)
Diabetes, n (%)	4 (13.8%)
Cirrhosis, n (%)	1 (3.4%)
Baseline SCr (mg/dL), median [IQR]	0.84 [0.71, 1.11]
Baseline eGFR (mL/min/1.73 m^2), mean (SD)	76.1 (20.3)
CKD, n (%)	
CKD Stage 1	11 (37.9%)
CKD Stage 2	11 (37.9%)
CKD Stage 3a	5 (17.2%)
CKD Stage 3b	1 (3.4%)
CKD Stage 4	1 (3.4%)
Medication use	
Diuretics	13 (43.3%)
ACEi/ARB	4 (13.3%)
Proton Pump Inhibitors	8 (2.7%)
Antibiotics	1 (0.3%)
NSAID	7 (23.3%)

Abbreviations: SCr=serum creatinine; eGFR= estimated glomerular filtration rate using CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration); SD=standard deviation; IQR=interquartile range; CKD= chronic kidney disease; ACEi=Angiotensin-converting-enzyme inhibitors; ARB= Angiotensin receptor blockers; NSAID= Non-Steroidal Anti-Inflammatory Drugs

The table showcases the hazard ratio of developing AKI stratified by sex, hypertension, diabetes, base line SCr and eGFR.

Table S2. *Univariate Associations between Baseline Patient Characteristics and Progression to AKI*

Baseline Characteristic	HR (95% CI)	*P*-value
Age at treatment initiation (years)	1.02 (0.96-1.08)	0.61
Sex	-	-
Male	0.73 (0.24-2.24)	0.59
Female	REF	REF
Hypertension	1.58 (0.53-4.73)	0.41
Diabetes	0.41 (0.05-3.17)	0.39
Baseline SCr (mg/dL)	2.08 (0.68-6.41)	0.20
Baseline eGFR (mL/min/1.73 m^2)	0.98 (0.96-1.003)	0.09

Abbreviations: SCr=serum creatinine, eGFR=estimated glomerular filtration rate; HR=hazard ratio; CI=confidence interval.

P-values were derived using univariable cox regression models.

P-values in bold denote statistical significance at the 0.05 alpha level.

Race, chronic liver disease, and CKD stage were not analyzed to sparse numbers.

Epidemiological characteristics of the cohort, including the average age, distribution of sexes, and the distribution based on chronic diseases and baseline laboratory values.

***Table S3**. Cumulative Incidence Estimates of AKI with Death as a Competing Risk*

Follow-up (months)	Cumulative Incidence of AKI	Cumulative Incidence of Death
1	10.3%	3.5%
2	13.8%	3.5%
3	28.9%	7.4%
4	28.9%	11.4%
5	28.9%	11.4%
6	37.4%	15.7%
7	46.0%	15.7%
8	46.0%	15.7%
9	50.2%	15.7%
10	50.2%	15.7%
11	50.2%	15.7%
12	50.2%	20.5%

Abbreviations: AKI= acute kidney injury

Table S4. *Predicted eGFR levels after capmatinib therapy initiation using a linear mixed model framework.*

Follow-up (months)	eGFR estimate (95% CI)[a], mL/min/1.73 m2
0	73.5 (66.5, 81.1)
1	65.7 (58.9, 73.6)
2	61.8 (55.2, 69.4)
3	64.8 (57.8, 72.2)
4	67.7 (60.1, 75.5)
5	66.3 (59.0, 73.7)
6	64.2 (57.2, 71.7)
7	63.7 (56.3, 71.5)
8	64.8 (56.9, 71.9)
9	66.2 (58.8, 73.7)
10	67.0 (59.7, 73.9)
11	66.2 (58.0, 73.5)
12	64.2 (54.7, 73.7)

Abbreviations: eGFR= estimated glomerular filtration rate; CI= confidence interval.

A 95% CI for the mean predicted value at a given time was estimated using the bootstrapping method

Supplementary Figures

Figure S1*. Flowchart of Inclusion and Exclusion Criteria*

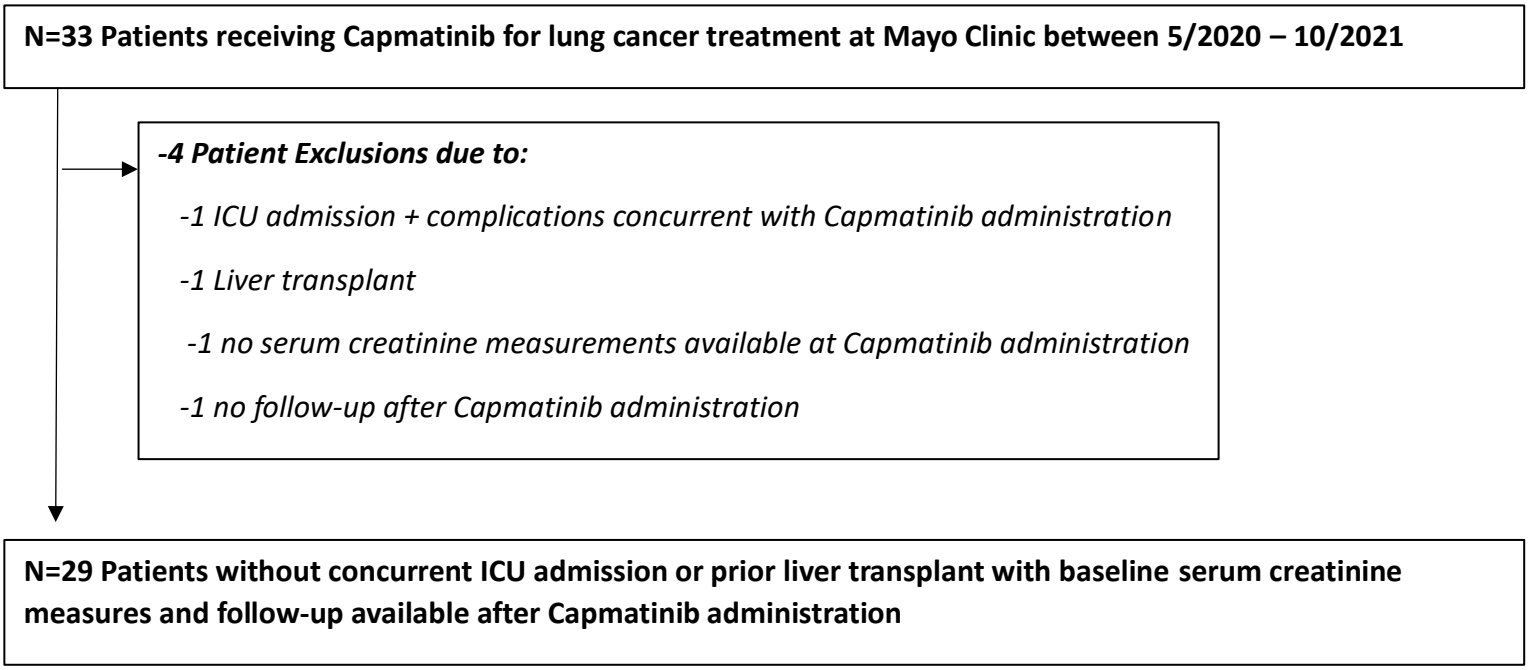
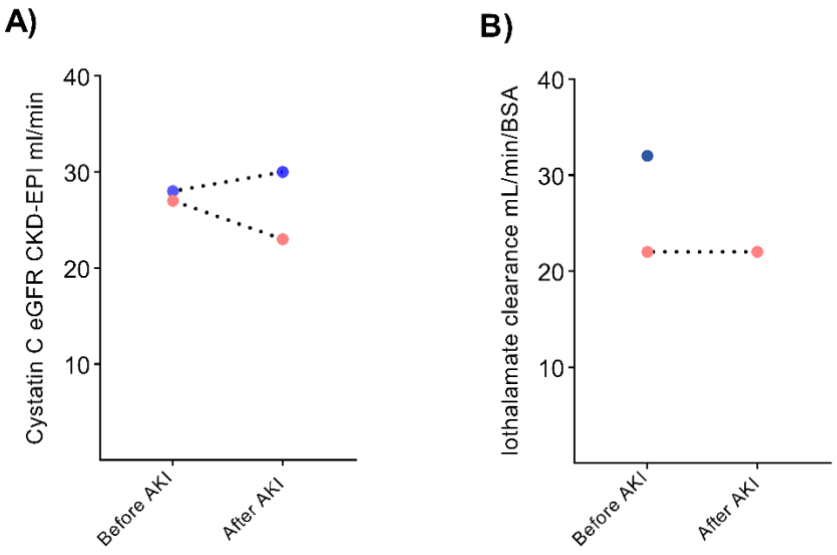
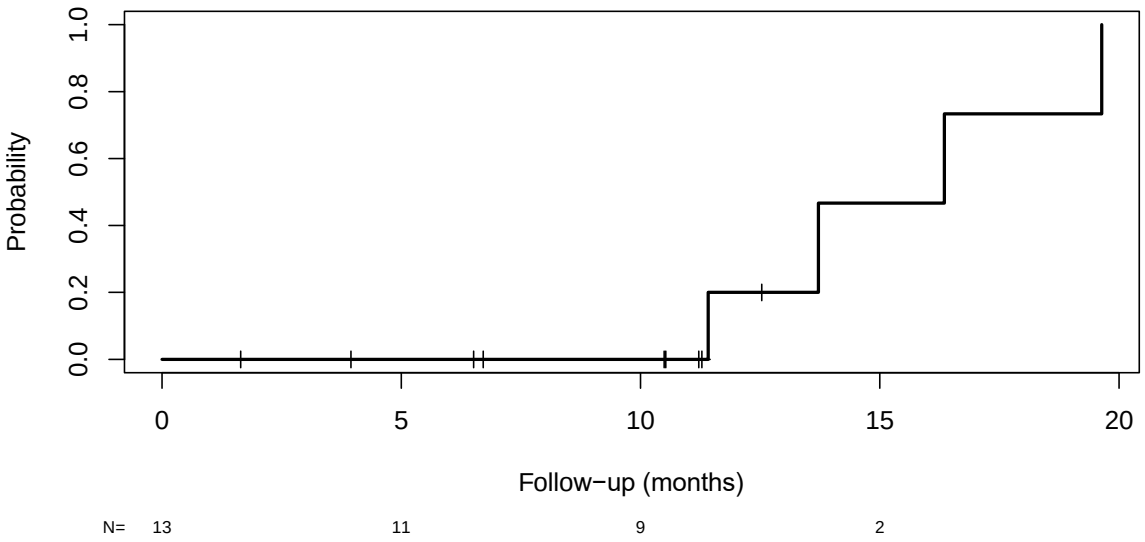


Figure S2. *Iothalamate and cystatin-c levels before and at the time of AKI*



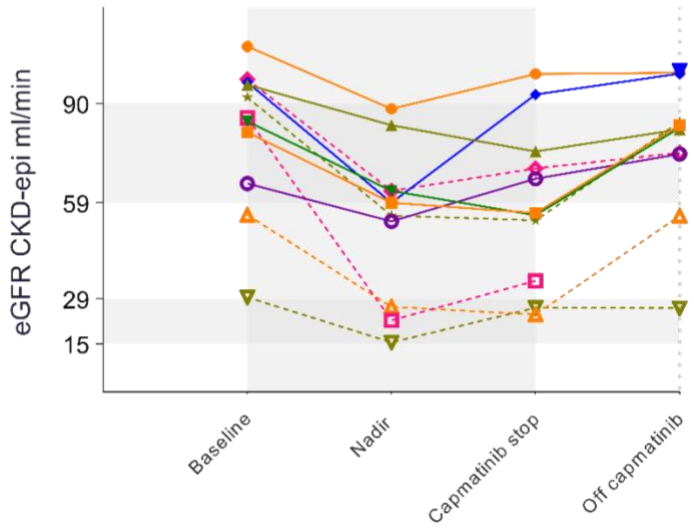
Patients are denoted in different colors. Panel A: cystatin c levels before and at the time of AKI (when available) and panel B: iothalamate clearance levels before and at the time of AKI. Dashed lines indicate each patient's trajectory.

Figure S3. *Cumulative incidence of death among patients with an AKI event*



Probability of all-cause mortality during capmatinib treatment in patients who had AKI event. The cumulative incidence (95% CI) estimates for death at 5-, 10-, and 15-months follow-up, respectively: 0%, 0%, 47%

Figure S4. *The plot of eGFR patient trajectories among patients that stopped capmatinib treatment*



eGFR trends among the 11 patients who stopped receiving capmatinib therapy. The grey vertical area indicates eGFR measurements taken while the patient received capmatinib treatment; the white area indicates eGFR measurements after the patient stopped receiving capmatinib therapy. Flat grey and white areas correspond to different CKD stages. Dashed lines indicate patients who developed AKI during capmatinib treatment; solid lines indicate patients who did not develop AKI during therapy.

Methods

We collected demographic data, clinical features, comorbidities, laboratory measurements, and clinical outcomes from 33 patients with NSCLC treated with capmatinib. Data was collected via manual chart review and was abstracted by two investigators trained in data collection using a standardized electronic data collection form. The Mayo Clinic, Institutional Review Board, approved all protocols. The ethics committee of the institution approved this retrospective cohort study.

The baseline was defined as the date of capmatinib treatment initiation. Baseline SCr values were defined as the closest SCr measure within two months before or at treatment initiation. Follow-up SCr measures within 12 months after treatment initiation and before the date of stopping capmatinib treatment were retained for analysis. Comorbidities were classified according to the International Classification of Disease (ICD). Chronic kidney disease was classified by Kidney Disease Improving Global Outcomes (KDIGO) criteria. Kidney function was estimated by the serum creatinine-based estimated glomerular filtration rate (eGFR) calculated by the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) 2021 race-free equation. AKI events were defined as a ≥1.5-fold increase in SCr levels from baseline or an increase of ≥0.3 mg/dL (grade 1 kidney toxicity). Time-to-incident AKI after initiating capmatinib therapy was considered the primary event of interest in time-to-event analyses, with death considered a competing risk. Patients were censored at the time of discontinuation of capmatinib treatment, end of study (12 months post-baseline), or last follow-up, whichever came first.

Cumulative incidence plots were estimated using cumulative incidence functions. The association between patient characteristics at baseline and incidence of AKI during follow-up was modeled using cause-specific Cox proportional hazards

regression models. The association between time since treatment administration and eGFR changes were modeled using linear mixed-effects models. *P*-values <0.05 were considered statistically significant. All analyses were performed using R version 4.0.3 or higher (R Foundation for Statistical Computing, Vienna, Austria).

Continuous variables were summarized using either mean, standard deviation (SD) for normally distributed distributions or median, interquartile range [IQR] for skewed distributions; categorical variables were summarized using n (%). Hazard ratios (HRs) and 95% confidence intervals (95% CIs) were presented for analyses using Cox proportional hazards regression models. Linear mixed models were fit with subject-specific intercepts and fixed effects for predictors to account for correlation between measures within the same patient. eGFR was suitable as a cubic spline term with seven degrees of freedom to capture any non-linearity between the time after treatment initiation and eGFR. Coefficient estimates and standard errors were reported from the mixed models. Predicted values and their associated 95% confidence intervals for the mean were also reported for eGFR measures across time after treatment initiation.

STROBE Statement

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	4	
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	N/A	
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3-4	
Objectives	3	State specific objectives, including any prespecified hypotheses	3-4	
Methods				
Study design	4	Present key elements of study design early in the paper	5	
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5	
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	5	
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	5	

Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6
Bias	9	Describe any efforts to address potential sources of bias	4-5
Study size	10	Explain how the study size was arrived at	N/A

Continued on next page

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5
		(*b*) Describe any methods used to examine subgroups and interactions	N/A
		(*c*) Explain how missing data were addressed	5
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	N/A
		(*e*) Describe any sensitivity analyses	N/A
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	Supplementary page 7
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Supplementary Pages 3-4
		(b) Indicate number of participants with missing data for each variable of interest	6
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	Figure 2

Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time		Figure 1
		Case-control study—Report numbers in each exposure category, or summary measures of exposure		N/A
		Cross-sectional study—Report numbers of outcome events or summary measures		N/A
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included		Figure 1
		(*b*) Report category boundaries when continuous variables were categorized		
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period		Supplementary Page 5
their analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A	
Discussion				
Key results	18	Summarise key results with reference to study objectives	8	
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	8-9	
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	N/A	
Generalisability	21	Discuss the generalisability (external validity) of the study results	9	
Other information				
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	N/A	

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.