Table 1: Prevalence and duration of kidney organ failure ('Standard exposure' group vs. 'High exposure' group)

	'Standard exposure' group (N=596)	'High exposure' group (N=604)	p-value
EstimatedGFR*:			
N. days (% of days from day 1 to 28 with values):			
Moderately-severely impaired: (eGFR: ≤60 mL/min/1.73 m^2)	3016 (43.4%)	3672 (48.1%)	<0.0001
Severely impaired: (eGFR ≤30 mL/min/1.73 m^2)	1445 (20.8%)	1910 (25.0%)	<0.0001
Severely impaired: (eGFR ≤30 mL/min/1.73 m^2), days from day 1 to 14	984 (20.0%)	1253 (23.5%)	<0.0001
'RIFLE' criteria, N patients (%) within day 1 to 28			
'R' reached	170 (28.5%)	209 (34.6%)	0.02
'I' reached	75 (12.6%)	92 (15.2%)	0.19
'F' reached	121 (20.3%)	150 (24.8%)	0.06
'R' or death	298 (50.0%)	327 (54.1%)	0.15
'I' or death	234 (39.3%)	252 (41.7%)	0.39
'F' or death	270 (45.3%)	287 (47.5%)	0.44
Urea			
Patients with a urea level ever ≥ 20 mmol/L (day 1-28); N (%)	217 (37.4%)	253 (43.4%)	0.04

*eGFR was assessed using the Cockcroft and Gault method [Ref: Cockcroft DW, Gault MH.: Prediction of creatinine clearance from serum creatinine. Nephron 1976;16:31-41]. Actual measured creatinin values were used. If using the 'last observation carried forward' approach regarding creatinin measurement to take into account that patients who died in renal failure should be counted as such, did not change the signal or the statistics of these analyses. 'R':Risk, 'I': Injury, 'F': Failure. Presence of renal failure according to 'RIFLE' was assessed using the guidelines developed by the acute dialysis quality initiative (www.adqi.net)

Table 2: Prevalence of kidney organ failure on the last day of follow-up ('Standard exposure' group vs. 'High exposure' group)

	'Standard exposure' group	'High exposure' group	p-value
Survivors and patients who had last creatinine measured>24 h before death:	**(N=432)**	**(N=438)**	
Renal failure (eGFR: ≤60 mL/min/1.73 m^2)	119 (27.6%)	137 (31.3%)	0.23
Patients who died (with last creatinine measured within 24 h before death):	**(N=150)**	**(N=145)**	
Renal failure (eGFR: ≤60 mL/min/1.73 m^2)	105 (70.0%)	99 (68.3%)	0.83
All patients with creatinine measurements	**(N=582)**	**(N=583)**	
Renal failure (eGFR: ≤60 mL/min/1.73 m^2)	224 (38.5)	236 (40.5)	0.51

*eGFR was assessed using the Cockcroft and Gault method [Ref: Cockcroft DW, Gault MH.: Prediction of creatinine clearance from serum creatinine. Nephron 1976;16:31-41]. Actual measured creatinin values were used.

Table 3. Multiple effects models investigating estimated GFR changes after starting and stopping beta-lactam antibiotics

		Unadjusted analysis		Multivariable analysis	
	Variable	**Regression coefficient (95% CI)**	**P-value**	**Regression coefficient (95% CI)**	**P-value**
After starting the drug					
Piperacillin/tazobactam	Per day more on piperacillin/tazobactam	1.39 (1.17, 1.60)	<0.0001	0.99 (0.71, 1.27)	<0.0001
Meropenem	Per day more on meropenem	2.74 (2.39, 3.09)	<0.0001	2.86 (2.45, 3.28)	<0.0001
Cefuroxim	Per day more on cefuroxim	1.91 (1.67, 2.16)	<0.0001	1.27 (0.90, 1.64)	<0.0001
After stopping the drug					
Piperacillin/tazobactam	Per day after stopping piperacillin/tazobactam	2.79 (2.35, 3.24)	<0.0001	2.70 (2.26, 3.14)	<0.0001
Meropenem	Per day after stopping meropenem	0.20 (-0.51, 0.91)	0.59	0.17 (-0.52, 0.86)	0.63
Cefuroxim	Per day after stopping cefuroxim	0.13 (-0.25, 0.50)	0.51	0.01 (-0.35, 0.37)	0.96

All multivariable analyses were adjusted for: treatment arm ('low exposure' vs. 'high exposure'), gender, age (≥65 vs. <65 years), APACHE II score (≥20 vs. <20), Clinically judged infection (severe sepsis/septic shock vs. milder or no infection), patient category (surgical vs. medical) and eGFR level at administration of the antibiotic, (1: <30 ml/min/1,73 m^2, 2: 31-60 ml/min/1,73 m^2, 3: >60 ml/min/1,73 m^2).

Table 4. Multivariable logistic regression: beta-lactam antibiotics and other risk variables vs. binary endpoint eGFR<60 ml/min/1.73m^2 on day 7.

	Unadjusted analysis		Multivariable analysis	
Variable	**Odds ratio (95% CI)**	**P-value**	**Odds ratio (95% CI)**	**P-value**
Other variables				
Age (≥65 vs. <65 years)	2.36 (1.86, 3.00)	<0.0001	1.85 (1.31, 2.60)	<0.0001
APACHE II score (≥20 vs. <20)	2.49 (1.90, 3.25)	<0.0001	1.64 (1.12, 2.41)	0.01
Severe sepsis/septic shock vs. milder or no infection	2.02 (1.59, 2,56)	<0.0001	1.16 (0.82, 1.66)	0.40
Auto-immune disease (Y vs. N)	1.31 (0.73, 2.33)	0.36	NI	-
Cancer (Y vs. N)	1.26 (0.88, 1.79)	0.21	NI	-
Charlson score (≥2 vs. <2)	1.72 (1.35, 2.18)	<0.0001	1.70 (1.21, 2.40)	0.002
Surgical (Y vs. N)	1.16 (0.90, 1.50)	0.24	NI	-
Body Mass Index (≥25 vs. <25)	1.57 (1.17, 2.12)	0.003	1.19 (0.78, 1.82)	0.41
Gender (Male vs. Female)	1.25 (0.99, 1.57)	0.06	1.28 (0.92, 1.78)	0.14
eGFR level at baseline				
>60 ml/min/1,73 m^2	Ref	-	Ref	-
31-60 ml/min/1,73 m^2	14.6 (10.2, 21.0)	<0.0001	11.7 (8.0, 17.0)	<0.0001
<30 ml/min/1,73 m^2	81.1 (51.2, 128.5)	<0.0001	65.9 (40.7, 106.6)	<0.0001
Beta-lactam antibiotics				
Piperacillin/tazobactam (≥3 vs. <3 days)*	2.32 (1.82, 2.96)	<0.0001	1.70 (1.18, 2.43)	0.004
Meropenem (≥3 vs. <3 days)*	0.99 (0.71, 1.37)	0.94	NI	-
Cefuroxim (≥3 vs. <3 days)*	0.73 (0.57, 0.94)	0.01	1.24 (0.85, 1.80)	0.26

All variables entered in the multivariable analysis were adjusted for the other variables in this model. *All beta-lactam drug exposures are (≥3 vs. <3 days within the first 7 days in the study). All variables with a p-value <0.2 were included in the multivariable model. NI: Not Included.