Renal toxicity following PTCy-CsA GVHD prophylaxis for matched donor stem cell transplant

Retrospective single-centre cohort study · 2015–2024 · n = 113

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Art by Lola-Anne Davis

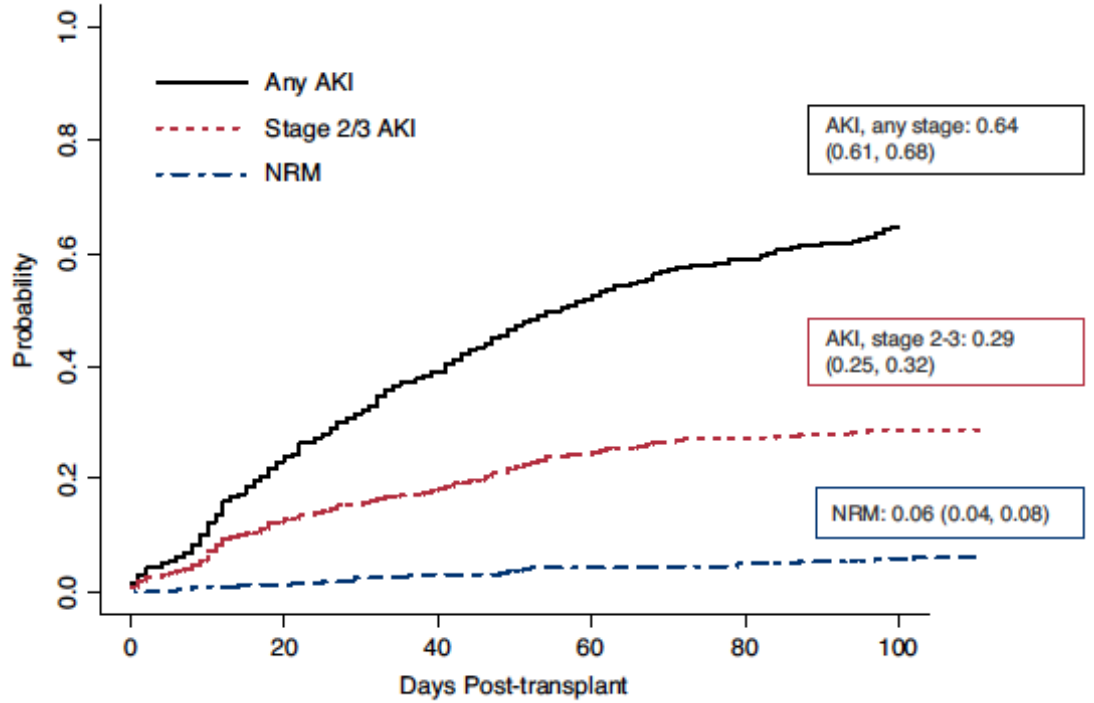
Disclosures

No conflict of interest to disclose

Acute kidney injury is common after HSCT

AKI stage	Serum Creatinine criteria	Urine output criteria
1	SCr increase ≥26 µmol/L within 48 hrs or SCr increase ≥1.5–2 fold from baseline	<0.5 mL/kg/hr for 6 consecutive hrs
2	SCr increase ≥2–3 fold from baseline	<0.5 mL/kg/hr for 12 hrs
3	SCr increase ≥3 fold from baseline or SCr increase ≥354 µmol/L or initiated on RRT (irrespective of stage at time of initiation)	<0.3 mL/kg/hr for 24 hr or anuria for 12 hr

eGFR < 35 (pediatrics)



Heterogeneous patient cohort

AKI is one of the most common early complications following transplantation

KDIGO criteria (Creatinine change) may not be suitable for BMT

- Baseline renal function may be abnormal – harder for Creatinine to double/triple
- Fluid shifts and loss of muscle mass lower creatinine

Abramson et al., CJASN 2021 (n = 616)

Acute Kidney Injury in Allogeneic HCT with Post-Transplant Cyclophosphamide

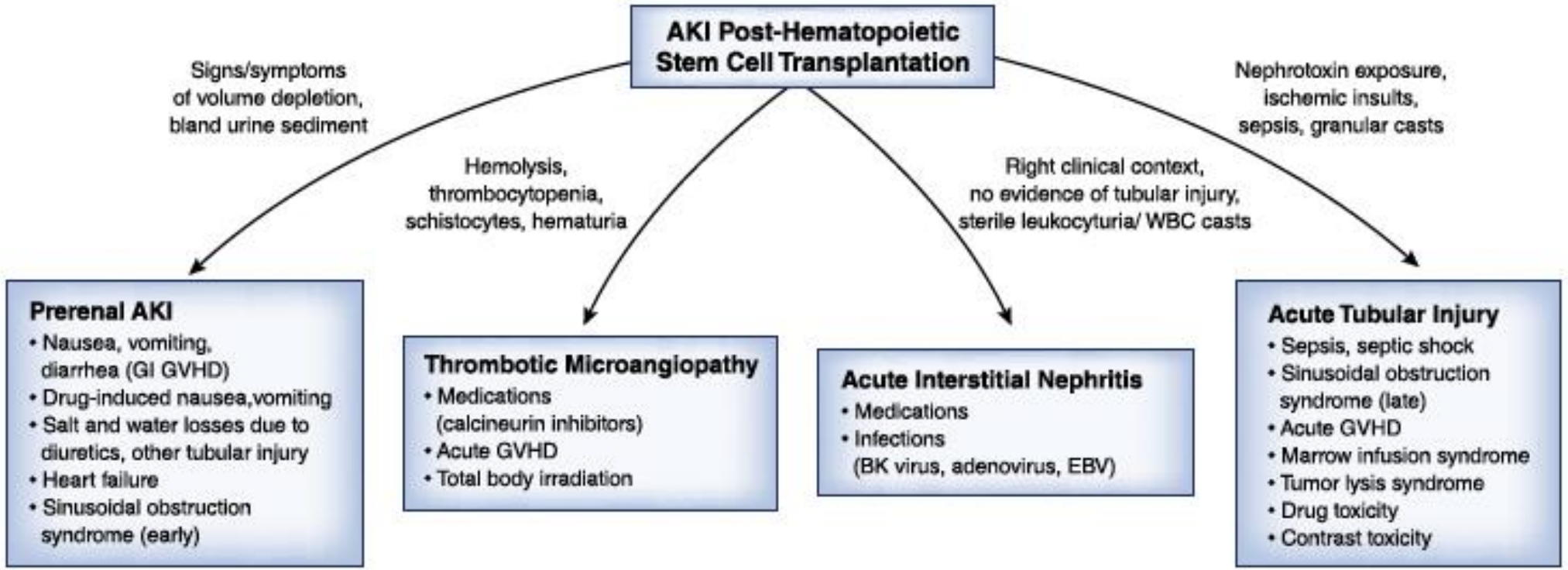
Table 2. Incidence of Acute Kidney Injury in the First 30 Days Post-HCT, Renal Recovery by D+90, and 100-Day Overall Survival

Baseline Kidney Function	**FK / MTX (N = 117)**	**PTCy-Based Regimen (N = 37)**	**All (N = 154)**	***p* value**
SCr, mg/dL, Median (Range)	0.75 (0.40-1.32)	0.84 (0.39-1.50)	0.78 (0.39-1.50)	0.061
eGFR, mL/min/1.73 m^2, Median (Range)	102 (66-144)	101 (52-144)	102 (52-144)	0.101
Acute Kidney Injury	**FK / MTX (N = 117)**	**PTCy-Based Regimen (N = 37)**	**All (N = 154)**	
Total AKI, n (%)	55 (47.0)	7 (18.9)	62 (40.3)	0.002
Stage 1, n (%)	24 (20.5)	4 (10.8)	28 (18.2)	
Stage 2, n (%)	21 (17.9)	1 (2.7)	22 (14.3)	
Stage 3, n (%)	4 (3.4)	1 (2.7)	5 (3.2)	
Dialysis, n (%)	6 (5.1)	1 (2.7)	7 (4.5)	
Renal Recovery by Day +90	**FK / MTX (N = 55)**	**PTCy-Based Regimen (N = 7)**	**All (N = 62)**	
Total Renal Recovery, n (%)	34 (61.8)	6 (85.7)	40 (64.5)	0.213
Stage 1, n (%)	21 (38.2)	3 (42.9)	24 (38.7)	
Stage 2, n (%)	10 (18.2)	1 (14.3)	11 (17.7)	
Stage 3, n (%)	1 (1.8)	1 (14.3)	2 (3.2)	
Dialysis, n (%)	2 (3.6)	1 (14.3)	3 (4.8)	
Between Group 100-Day Overall Survival Stratified by AKI and Stage	**FK / MTX**	**PTCy-Based Regimen**	**All**	
No AKI, n/N (%)	58/62 (93.5)	29/30 (96.7)	87/92 (94.6)	0.536
AKI, n/N (%)	45/55 (81.8)	6/7 (85.7)	51/62 (82.3)	0.799
Stage 1, n/N (%)	23/24 (95.8)	4/4 (100.0)	27/28 (96.4)	
Stage 2, n/N (%)	17/21 (81.0)	1/1 (100.0)	18/22 (81.8)	
Stage 3/Dialysis, n/N (%)	5/10 (50.0)	1/2 (50.0)	6/12 (50.0)	

Abbreviations: AKI, acute kidney injury; eGFR, estimated glomerular filtration rate; FK, tacrolimus; MTX, methotrexate; PTCy, post-transplant cyclophosphamide; SCr, serum creatinine

Myers et al., ASTCT 2025

Potential causes of Acute kidney injury



Renaghan CJSAN 2019

Questions

1. What is the incidence of AKI with the PTCy-CsA regimen?
2. What risk factors predict AKI?
3. Is AKI associated with worse transplant outcomes?

Methods

Cohort

113 adult alloHSCT recipients, 2015–2024 · PTCy–cyclosporine GVHD prophylaxis (PTCy 50 mg/kg D+3/+4, CsA from D+5 at 2 mg/kg IV, levels checked weekly with dose adjustment)

Renal function

eGFR by CKD-EPI 2009, BSA-adjusted (mL/min/1.73 m^2)

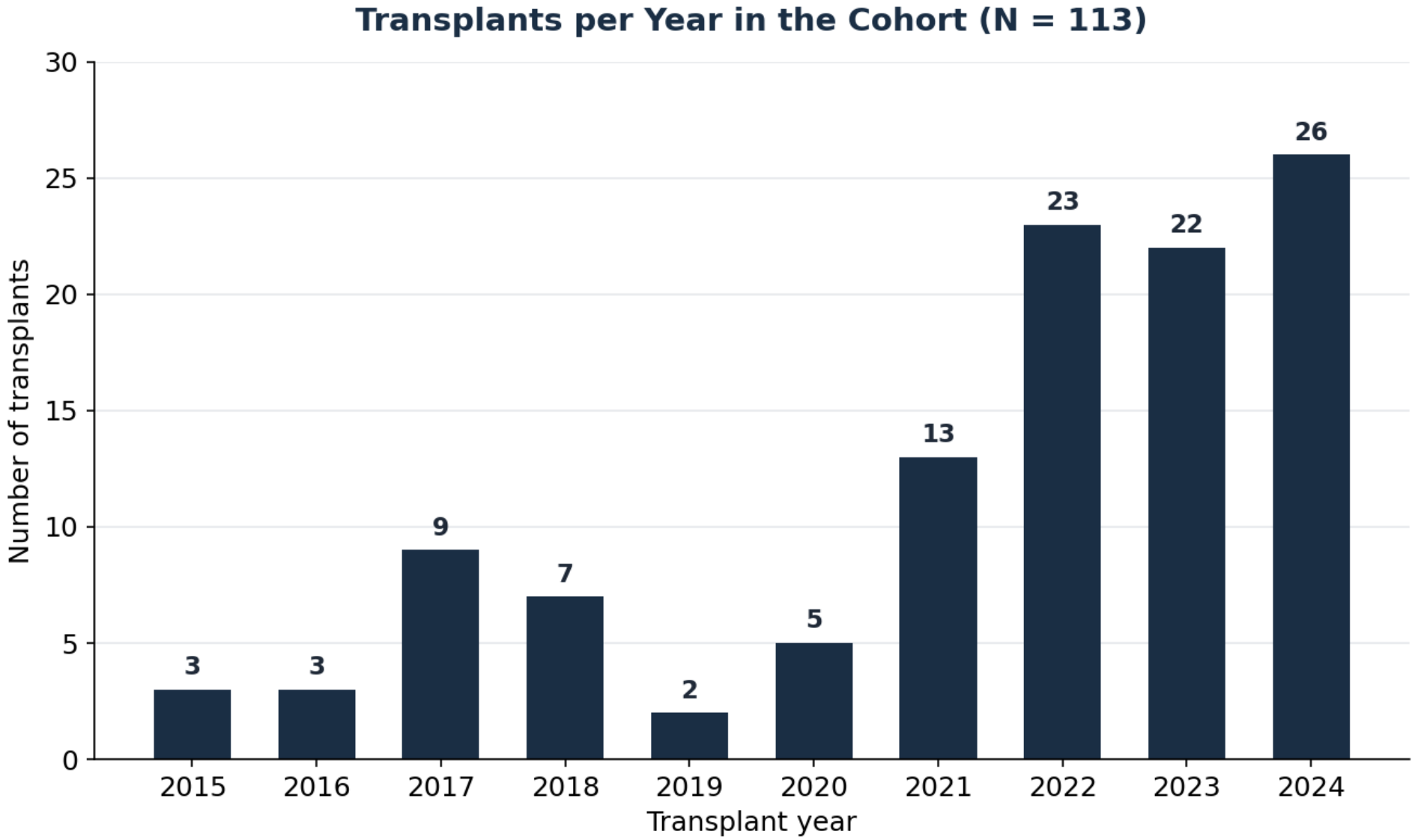
AKI grading

KDIGO criteria, 7-day rolling ≥1.5× baseline (48-hour criterion omitted — sampling approximately weekly) · records reviewed for reason for CsA cessation and conversion to renal-sparing immunosuppression

Analysis

Descriptive statistics including cumulative incidence and multivariable analysis

Results


Transplants per Year in the Cohort (N = 113)
Number of transplants
Transplant year
0
5
10
15
20
25
30
2015
2016
2017
2018
2019
2020
2021
2022
2023
2024
3
3
9
7
2
5
13
23
22
26

Baseline characteristics

113 patients underwent renal function assessment before and after transplant — median age 60 yr, 70% male.

Primary diagnosis

AML	65	58%
MDS	23	20%
ALL	22	19%
SAML	3	3%

Renal function at baseline

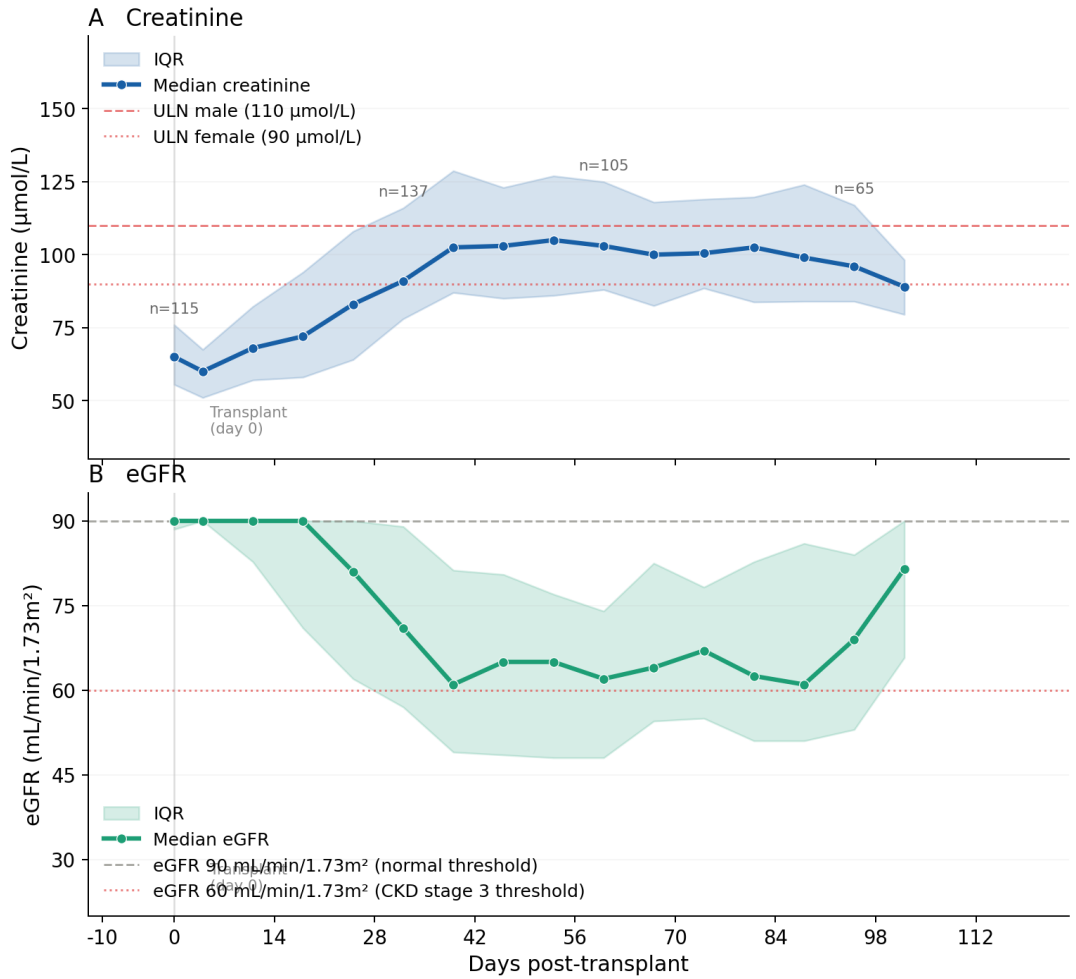
Median serum creatinine was **68.0 µmol/L**, corresponding to a median CKD-EPI eGFR (BSA-adjusted) of **105.5 mL/min/1.73m²** — within the normal range for the cohort as a whole.

"Renal function was preserved at baseline across the cohort."

Baseline characteristics

Characteristic	Overall (n=113)
Demographics	
Age, yr — median (IQR)	60 (51–66)
Sex — male / female, n (%)	79 (70%) / 34 (30%)
Disease characteristics	
AML	65 (58%)
MDS	23 (20%)
ALL	22 (19%)
Other	3 (3%)
Transplant characteristics	
Matched unrelated donor	74 (61%)
Reduced intensity conditioning (RIC)	101 (83%)
Renal function	
Pre-conditioning creatinine, µmol/L	70 (62–80)
Pre-conditioning eGFR, mL/min/1.73m²	95 (85–102)
Day 0 creatinine, µmol/L	65 (56–75)
Day 0 eGFR, mL/min/1.73m²	97 (89–110)
CsA management	
Switched to sirolimus	22 (19%)
AKI 11· TMA/MAHA/haemolysis 6 · neurotoxicity 3 · other 2 (HTN, intolerance)	
ICU admission	14 (12%)

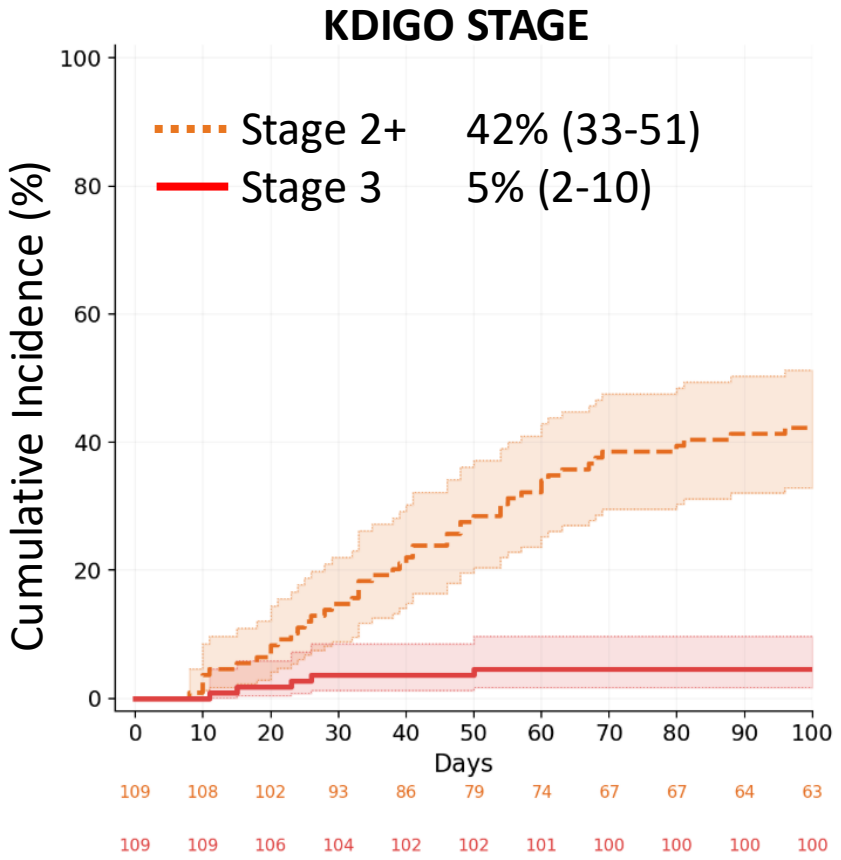
Renal function over time post-transplant
Median and IQR (n=113 patients)

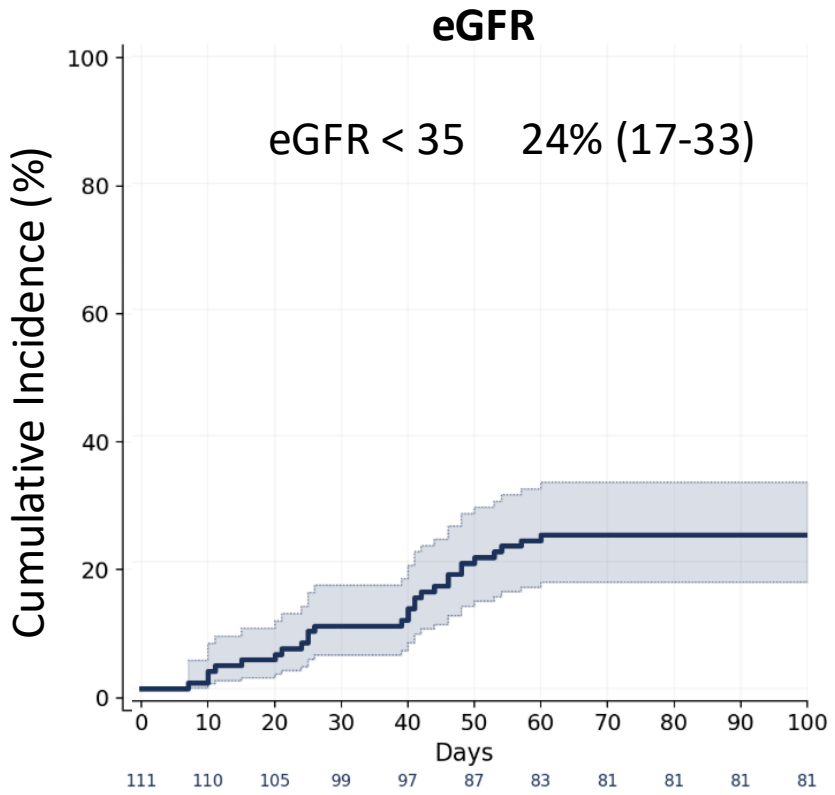


Median renal function declines around Day 40 and does not return to baseline by 12 months

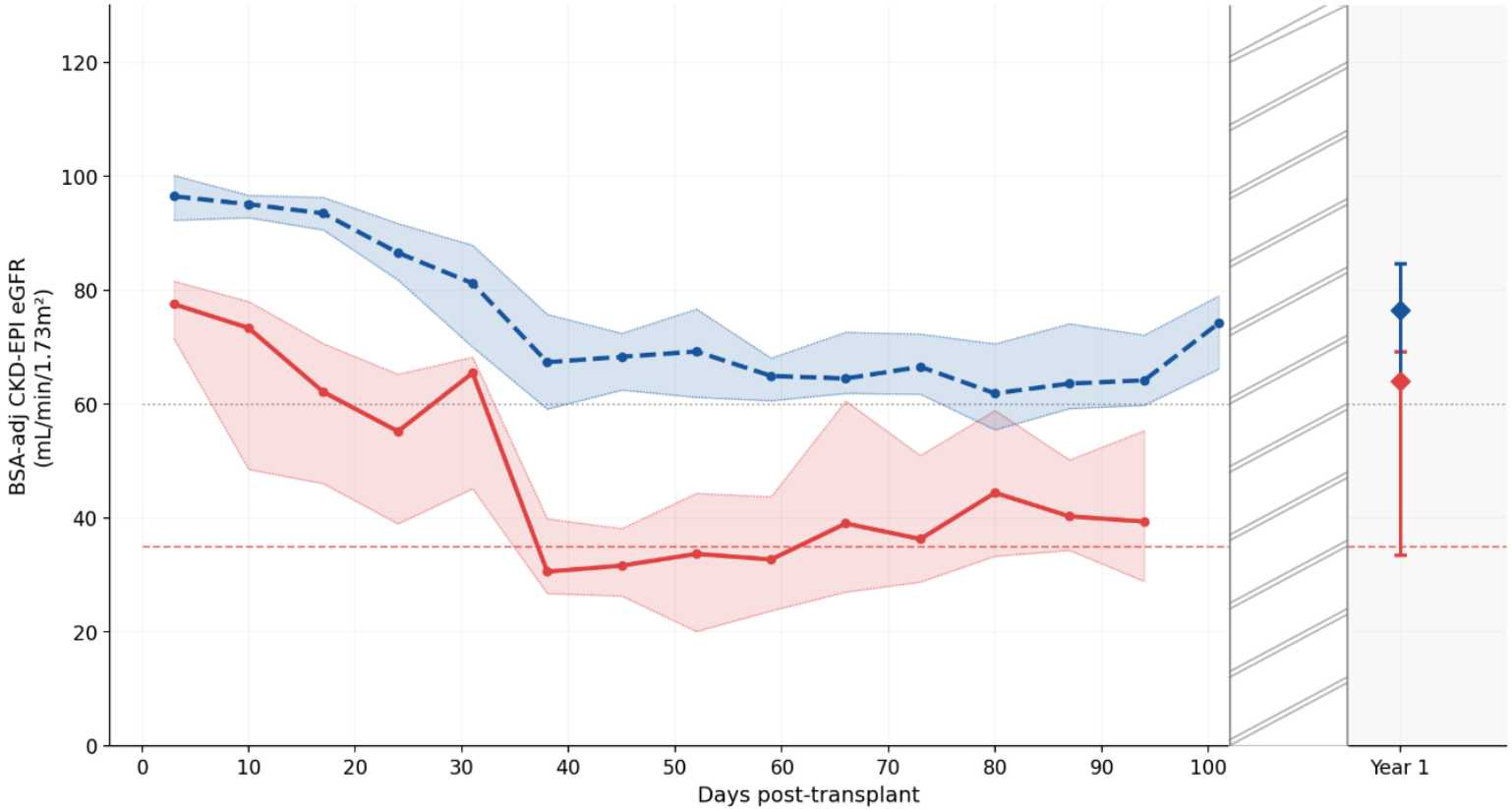
n= number of creatinine readings within each 7-day window. Patients lost to follow up (death, relapse) reduce n at later timepoints.

Cumulative incidence of renal failure





Long-term renal function

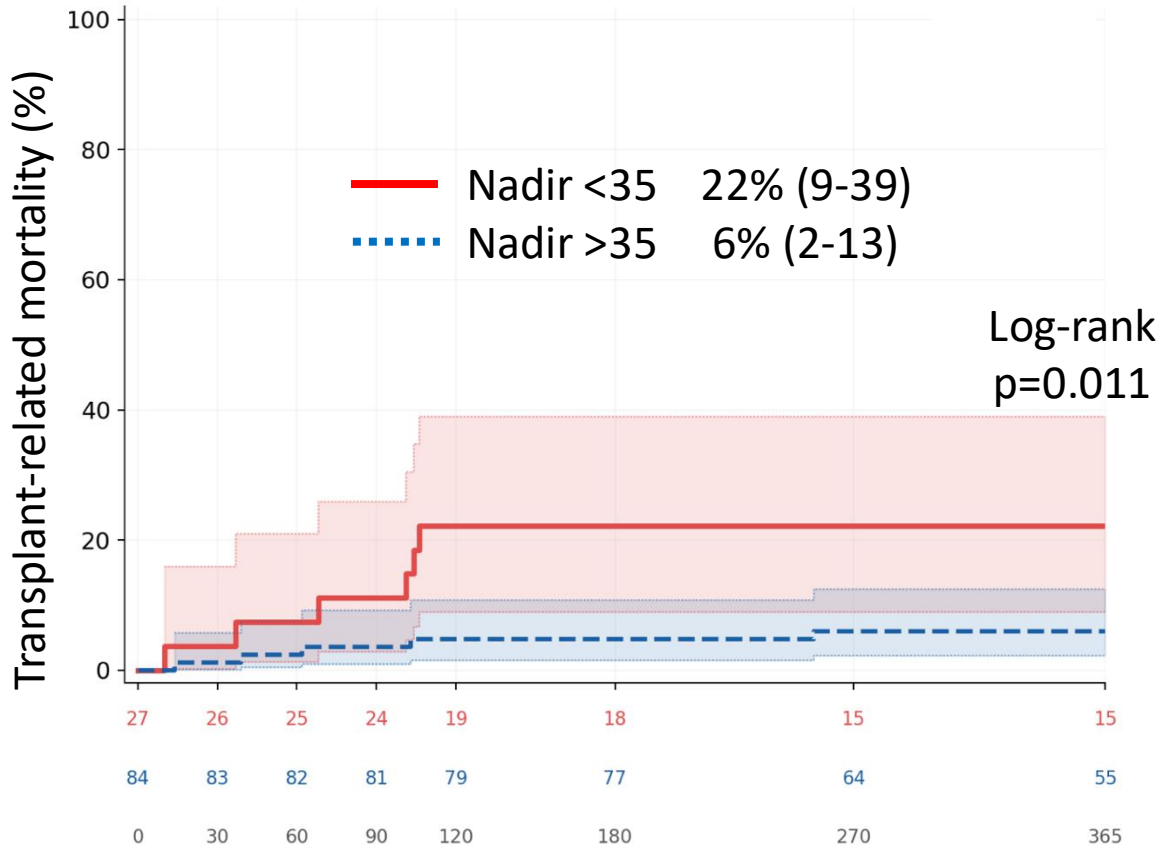


12 month

Nadir >35 (n=23) 76 mL/min (64-85)

Nadir <35 (n=11) 64 mL/min (34-69)

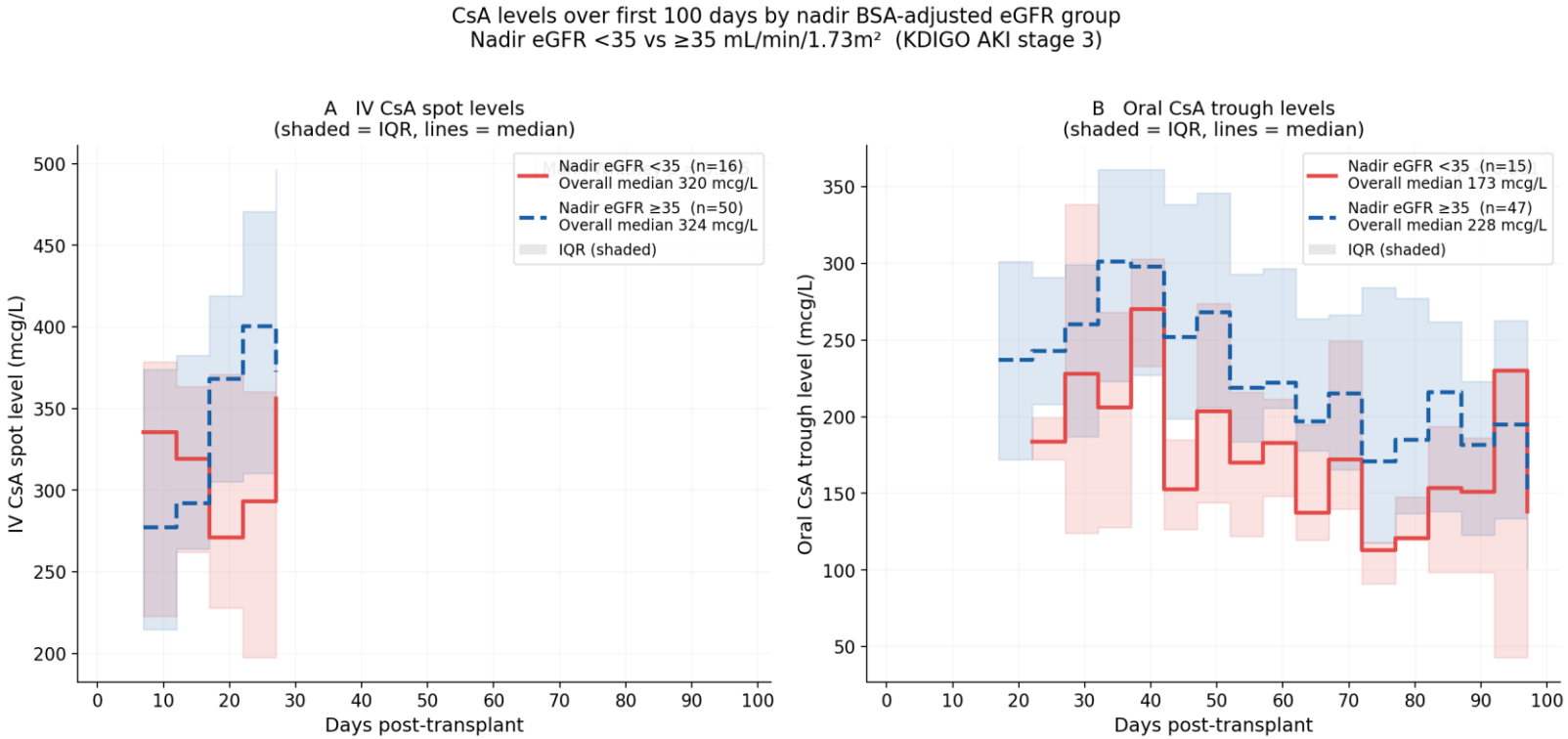
Nadir eGFR < 35 associated with increased 1-year transplant-related mortality



Characteristics of Patients with eGFR < 35

Characteristic	Nadir <35 (n=27)	Nadir ⩾35 (n=84)	p
Age, years	63 (57–66)	60 (50–65)	0.109
Male sex	22/27 (81%)	57/84 (68%)	0.174
Unrelated donor	19/27 (70%)	50/84 (60%)	0.312
MAC conditioning	2/27 (7%)	18/84 (21%)	0.099
AML	18/27 (67%)	49/84 (58%)	0.441
MDS	5/27 (19%)	17/84 (20%)	0.845
Pre-tx BSA-adj eGFR	**77 (66–83)**	**93 (83–103)**	**<0.001**
Day-0 BSA-adj eGFR	**77 (62–83)**	**96 (87–106)**	**<0.001**
Nadir BSA-adj eGFR	**27 (24–32)**	**50 (41–62)**	**<0.001**

eGFR<35 not associated with increased CsA levels

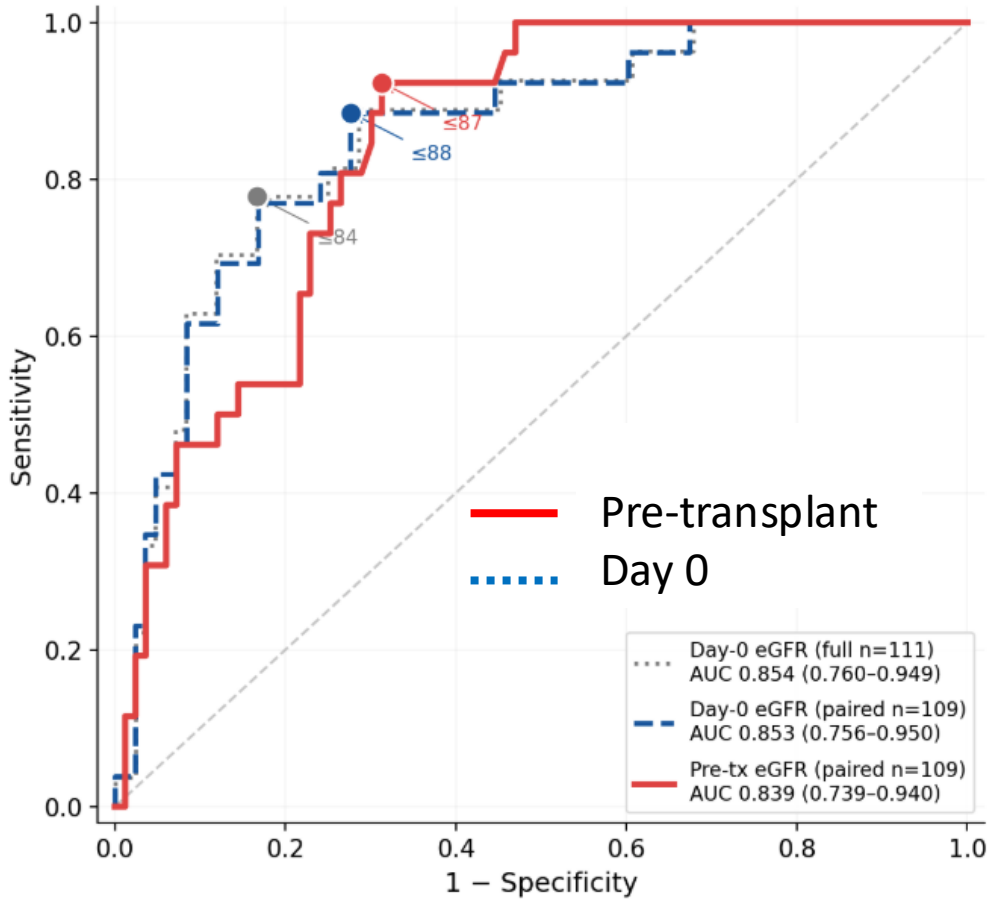


	Nadir <35	Nadir ≥35	p
IV spot (n=14 vs 47)	319 mcg/L	326 mcg/L	0.687
Oral trough (n=7 vs 39)	302 mcg/L	262 mcg/L	0.172

Multivariable analysis for eGFR < 35

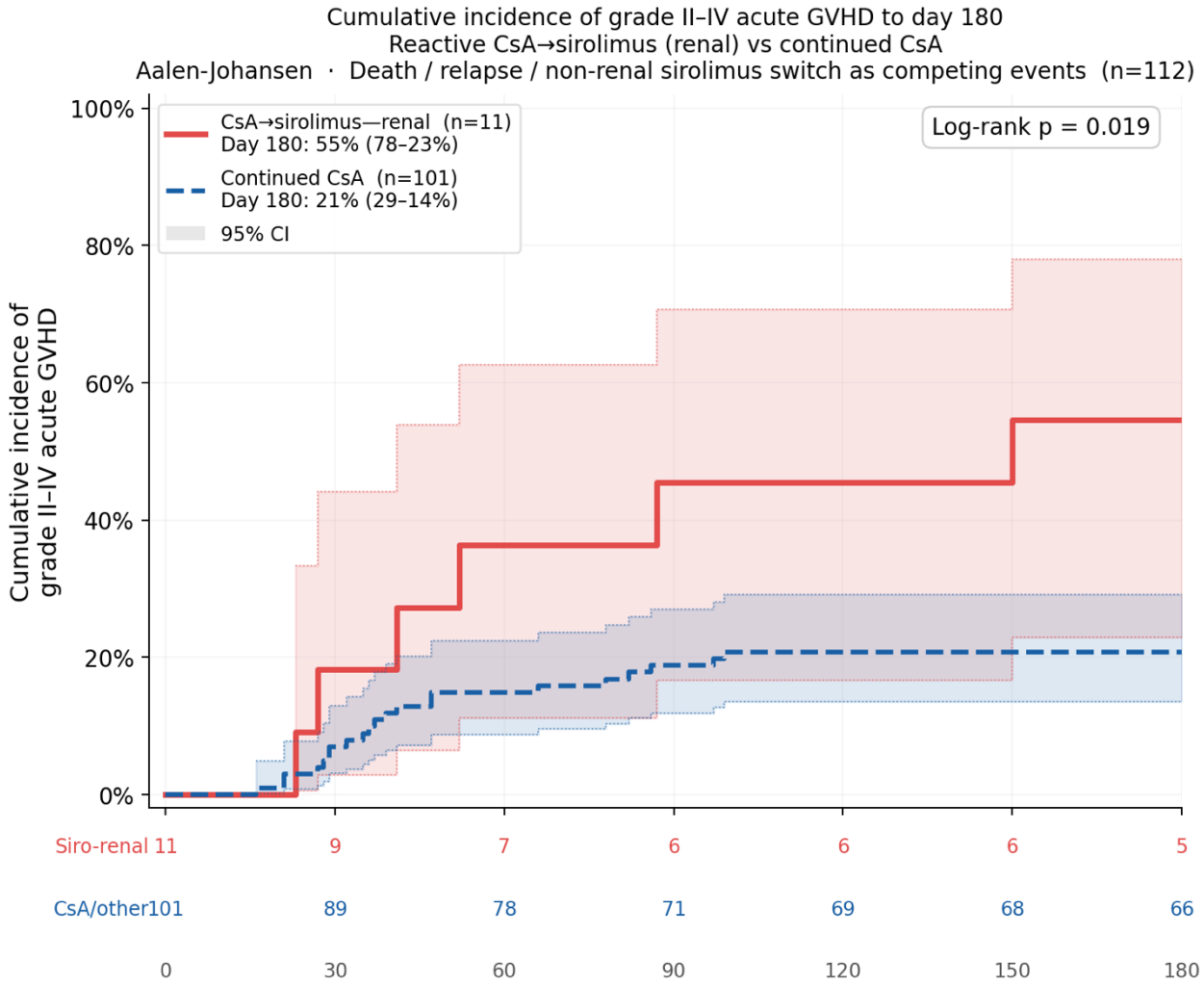
Predictor	Model A (Day-0)	Model B (Pre-tx)	Model C (Both)
Day-0 BSA-eGFR	**0.47 (0.33–0.68) p<0.001**	—	**0.56 (0.37–0.85) p=0.006**
Pre-tx BSA-eGFR	—	**0.42 (0.27–0.64) p<0.001**	0.62 (0.38–1.01) p=0.056
Age	1.02 NS	0.81 NS	0.98 NS
Male sex	1.21 NS	1.19 NS	0.87 NS
Unrelated donor	0.92 NS	1.10 NS	1.05 NS
MAC conditioning	1.66 NS	0.47 NS	2.23 NS
AML or MDS	1.40 NS	1.66 NS	1.57 NS

Day 0 BSA-eGFR best predictive value



	Pre-tx BSA-adj eGFR	Day-0 BSA-adj eGFR
AUC	**0.839** (0.739–0.940)	**0.853** (0.756–0.950)
Optimal threshold	⩽87 mL/min	⩽88 mL/min
Sensitivity	**92%**	88%
Specificity	69%	72%
Youden J	**0.610**	0.608
PPV at ⩽80	47%	**63%**
NPV at ⩽80	85%	**89%**
n eligible at ⩽80	30 (28%)	27 (25%)

Sirolimus and cumulative incidence acute GVHD



Implications of study

1. AKI is common with PTCy-CsA

- 42% of transplant recipients receiving PTCy-CsA Stage 2+ AKI

- 24% of those with AKI have CKD Stage 3b (eGFR < 35)

2. eGFR < 35 associated with higher NRM

3. Day 0 eGFR < 80 mL/min predicts at-risk

- PPV 63% and NPV 89%

- One quarter of transplant recipients

4. CsA likely contributor to AKI

- Argument for CNI-free regimens in those at risk

Limitations of study

1. **Retrospective single center study, requires validation**
2. **CsA dosing clinician dependent, contributing not causal**
3. **Other factors not considered – sepsis, antibiotics**
4. **Renal outcomes beyond 12months not known, or dialysis dependence**

Current Strategy at Alfred:
Pilot Study CNI-free GVHD regimen: PTCy + Abatacept

- **Rationale**
  - Avoid cyclosporin toxicity without compromising GVHD prophylaxis
- **Indication**
  - Matched donor allografts with pre-conditioning/or Day 0 eGFR CKD-EPI ≤80ml/min/1.73m^2 (maximum 10 per year)
- **Regimen (Koura et al, Blood Advances 2025)**
  - PTCy 40 mg/kg on D+3, D+4
  - Abatacept 10 mg/kg (max 1 g) on D+5, D+14, D+28, D+56, D+85, D+112, D+140 and D+168
  - Reported outcomes: Grade III–IV acute GVHD 4.2%; moderate–severe chronic GVHD 0%
- **Cost — approximately $8,000 per patient**

PLAN: **10 patients will undergo the pilot study, then re-evaluate.**

Questions?

Thank you!

"art washes away from the soul the dust of everyday life" – Pablo Picasso

Art by Lola-Anne Davis