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ACUTE KIDNEY INJURY ASSOCIATED WITH IMMUNE-CHECKPOINT INHIBITORS IN CANCER PATIENTS: A SINGLE CENTRE RETROSPECTIVE STUDY

JYOTHI KUPPA[1], NITESH RAO[1], RAJIV JUNEJA[1], CAROLINE MILTON[1]

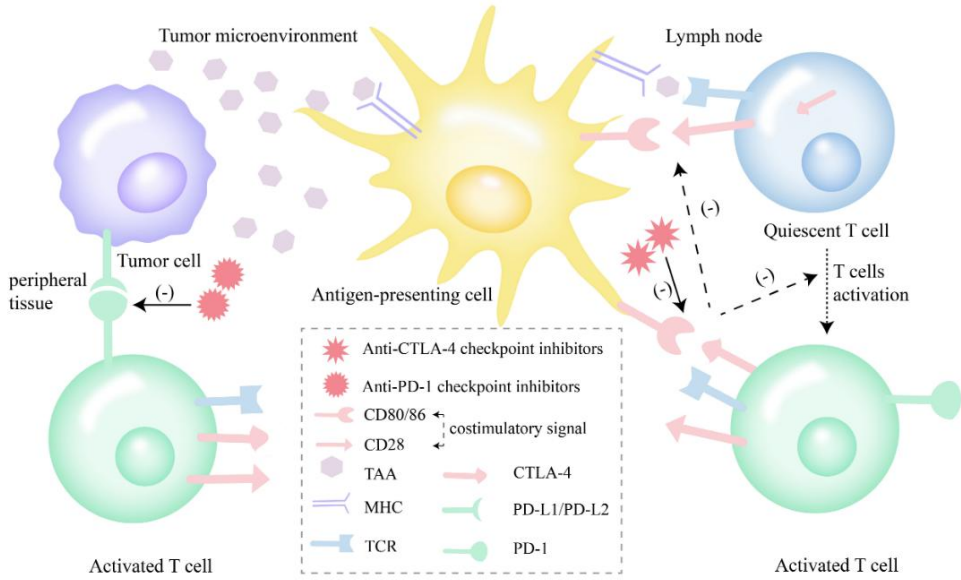
[1]Renal Unit, Flinders Medical Centre, Bedford Park, South Australia, Australia.

Background

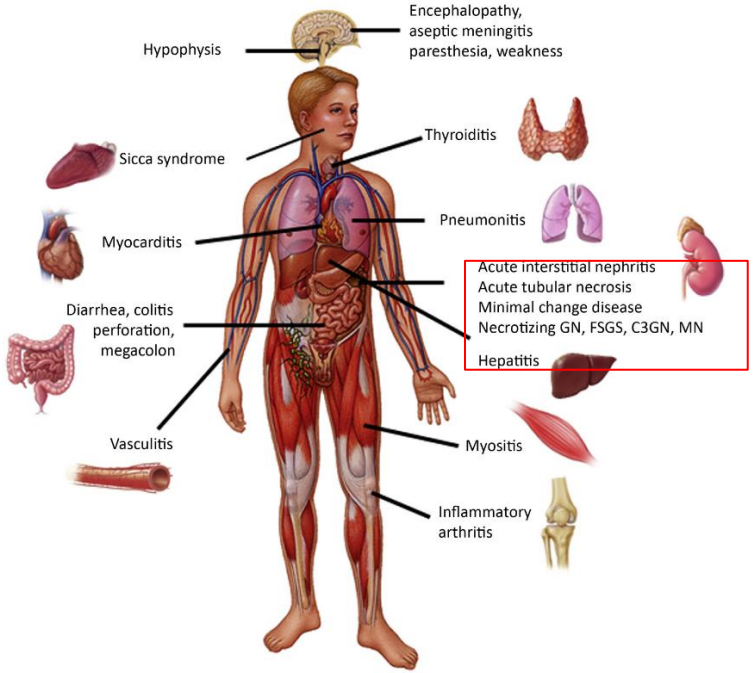
Monoclonal antibodies that target key immune checkpoint pathways – CTLA-4, PD-1 and PD-L1, resulting in enhanced tumour-directed immune responses

Mechanism is not selective and can cause immune related adverse effects (IRAEs), including AKI (ICI-AKI)

Limited Australian data, no South Australian data regarding ICI-AKI



Effects of ICIs on T-cell function[1]



Various organs affected in immune-mediated injury caused by immune checkpoint inhibitors[2]

Aim

- To examine and summarise the rates of ICI-AKI and their outcomes at Flinders Medical Centre (FMC), South Australia

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Methods

- Retrospective study
- Inclusion: adult patients who received anti-PD-1/PDL1/CTLA-4 therapy at FMC between 2020-2023
- Exclusions: on RRT, kidney transplant recipients, missing follow-up laboratory data
- Follow-up: 12 months post last cycle of ICI
- Definition of ICI-AKI:
  - ICI cycle delayed/discontinued for suspected ICI-AKI, OR
  - Kidney biopsy evidence of AIN, OR
  - Treatment administered for presumed ICI-AKI
- Statistical analyses: Wilcoxon, t-test and Chi-square tests for group comparison

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Results

507 patients included

58 (11.4%) developed AKI

11 (2.2% of the total cohort; 19% of AKI cases) were attributed to ICI-AKI

Characteristic	N	Overall N = 507[1]	No AKI N = 449[1]	AKI N = 58[1]	p-value[2]
Age at ICI initiation	507	69.0 (61.0, 76.0)	69.0 (61.0, 75.0)	72.0 (63.0, 77.0)	0.10
Sex	507				0.9
Male		293 (57.8%)	259 (57.7%)	34 (58.6%)	
Female		214 (42.2%)	190 (42.3%)	24 (41.4%)	
Type of ICI	507				
Atezolizumab		70 (13.8%)	65 (14.5%)	5 (8.6%)	0.2
Avelumab		15 (3.0%)	14 (3.1%)	1 (1.7%)	>0.9
Cemiplimab		6 (1.2%)	6 (1.3%)	0 (0.0%)	>0.9
Durvalumab		62 (12.2%)	60 (13.4%)	2 (3.4%)	0.030
Ipilimumab		68 (13.4%)	55 (12.2%)	13 (22.4%)	0.033
Nivolumab		197 (38.9%)	168 (37.4%)	29 (50.0%)	0.064
Pembrolizumab		158 (31.2%)	137 (30.5%)	21 (36.2%)	0.4
Combination therapy (CTLA-4 + PD-1/PD-L1)		65 (12.8%)	53 (11.8%)	12 (20.7%)	0.057
Baseline creatinine (µmol/L)	507	72.0 (58.0, 89.0)	71.0 (58.0, 88.0)	76.5 (64.0, 91.0)	0.2
Baseline eGFR (mL/min/1.73m^2)	507	87.0 (70.0, 90.0)	88.0 (71.0, 90.0)	84.0 (64.0, 90.0)	0.10

[1] Median (Q1, Q3); n (%)

[2] Wilcoxon rank sum test; Pearson's Chi-squared test; Fisher's exact test

Table 1: Baseline characteristics: AKI and no AKI

Characteristic	N	Overall N = 507[1]	No ICI-AKI N = 496[1]	ICI-AKI N = 11[1]	p-value[2]
Age at ICI initiation	507	69.0 (61.0, 76.0)	69.0 (61.0, 76.0)	73.0 (66.0, 75.0)	0.5
Sex	507				>0.9
Male		293 (57.8%)	287 (57.9%)	6 (54.5%)	
Female		214 (42.2%)	209 (42.1%)	5 (45.5%)	
Type of ICI	507				
Atezolizumab		70 (13.8%)	69 (13.9%)	1 (9.1%)	>0.9
Avelumab		15 (3.0%)	15 (3.0%)	0 (0.0%)	>0.9
Cemiplimab		6 (1.2%)	6 (1.2%)	0 (0.0%)	>0.9
Durvalumab		62 (12.2%)	62 (12.5%)	0 (0.0%)	0.4
Ipilimumab		68 (13.4%)	64 (12.9%)	4 (36.4%)	0.047
Nivolumab		197 (38.9%)	191 (38.5%)	6 (54.5%)	0.4
Pembrolizumab		158 (31.2%)	155 (31.3%)	3 (27.3%)	>0.9
Combination therapy (CTLA-4 + PD-1/PD-L1)		65 (12.8%)	62 (12.5%)	3 (27.3%)	0.2
Baseline creatinine (µmol/L)	507	72.0 (58.0, 89.0)	71.5 (58.0, 88.5)	89.0 (79.0, 101.0)	0.023
Baseline eGFR (mL/min/1.73m^2)	507	87.0 (70.0, 91.0)	88.0 (71.0, 91.0)	68.0 (59.0, 78.0)	0.007
[1]Median (Q1, Q3); n (%)					
[2]Wilcoxon rank sum test; Fisher's exact test					

Table 2: Baseline characteristics: ICI-AKI

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ICI-AKI – Baseline characteristics

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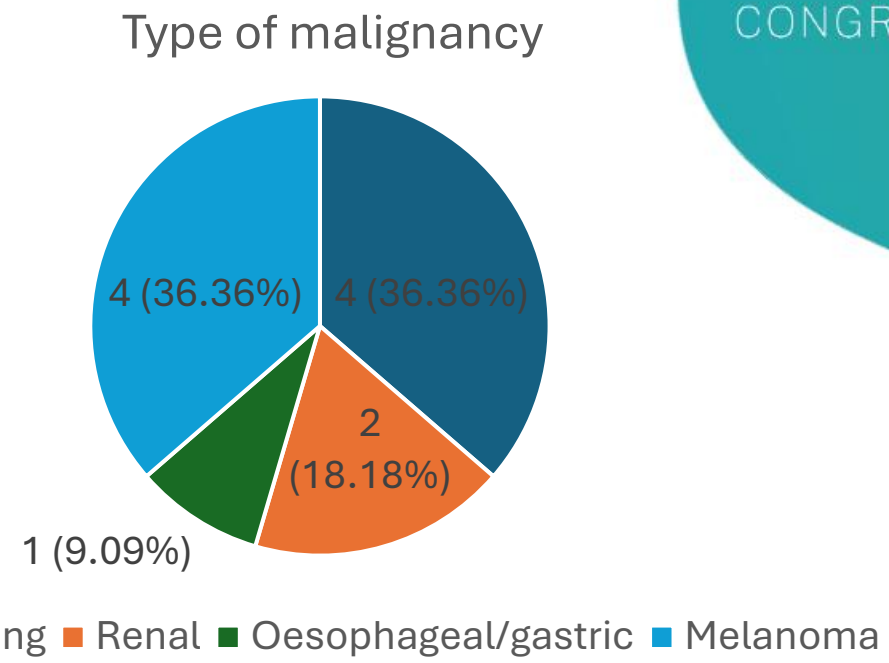
🧍 Demographics

- **Median age**: 73 years (66.0, 75.0)
- **Gender**:
  - Male: 6 (54.5%)
  - Female: 5 (45.5%)



💊 Concomitant Factors

- On PPIs: 3 (27.3%) + 1 unknown
- Non-renal IRAEs: 4 (36.4%)

Baseline eGFR (mL/min/1.73m^2): 68.0 (59.0, 78.0)

- CKD stage 5 (eGFR <15): 0 (0.0%)
- CKD stage 4 (eGFR 15-29): 2 (18.2%)
- CKD stage 3 (eGFR 30-60): 1 (9.1%)
- CKD stage 2 (eGFR 60-89): 6 (54.5%)
- CKD stage 1 (eGFR ≥90): 2 (18.2%)

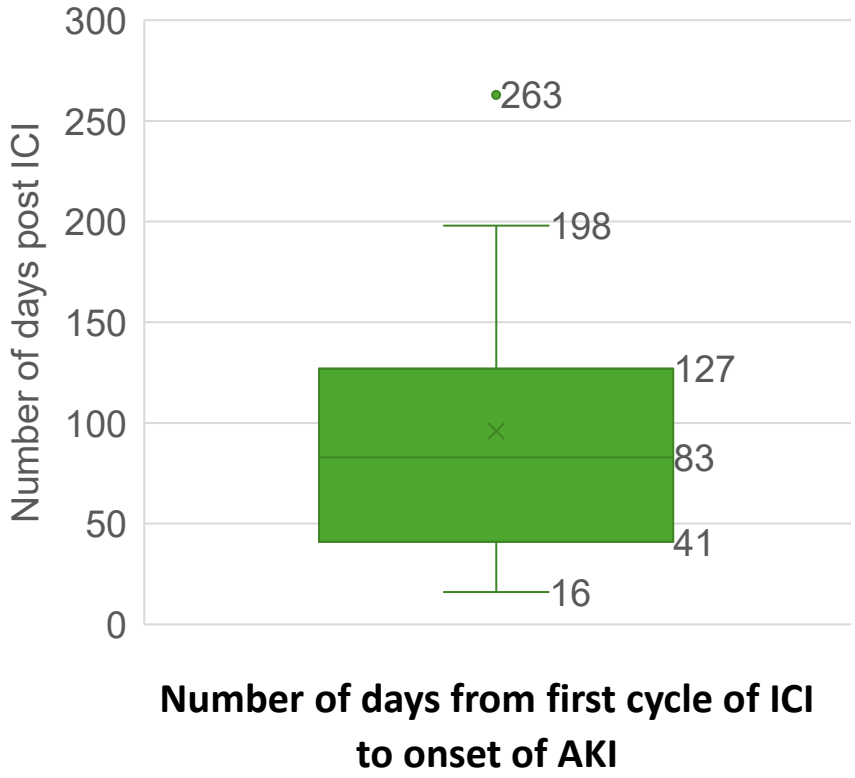
ICI-AKI – Clinical features

🚨 **AKI Characteristics**

- Median time to AKI onset (days): 83 (41, 127), after ~4 cycles

🦠 **Investigations**

- 70% had sterile pyuria
- Median urine ACR (mg/mmol) : 5.1 (n = 9)
- Biopsy performed: 4 (36.4%)
  - Findings:
    - 100% AIN
    - 75% with ATI
  - Median time to biopsy: 106 days post-AKI



Number of days from first cycle of ICI to onset of AKI

ICI-AKI – Management

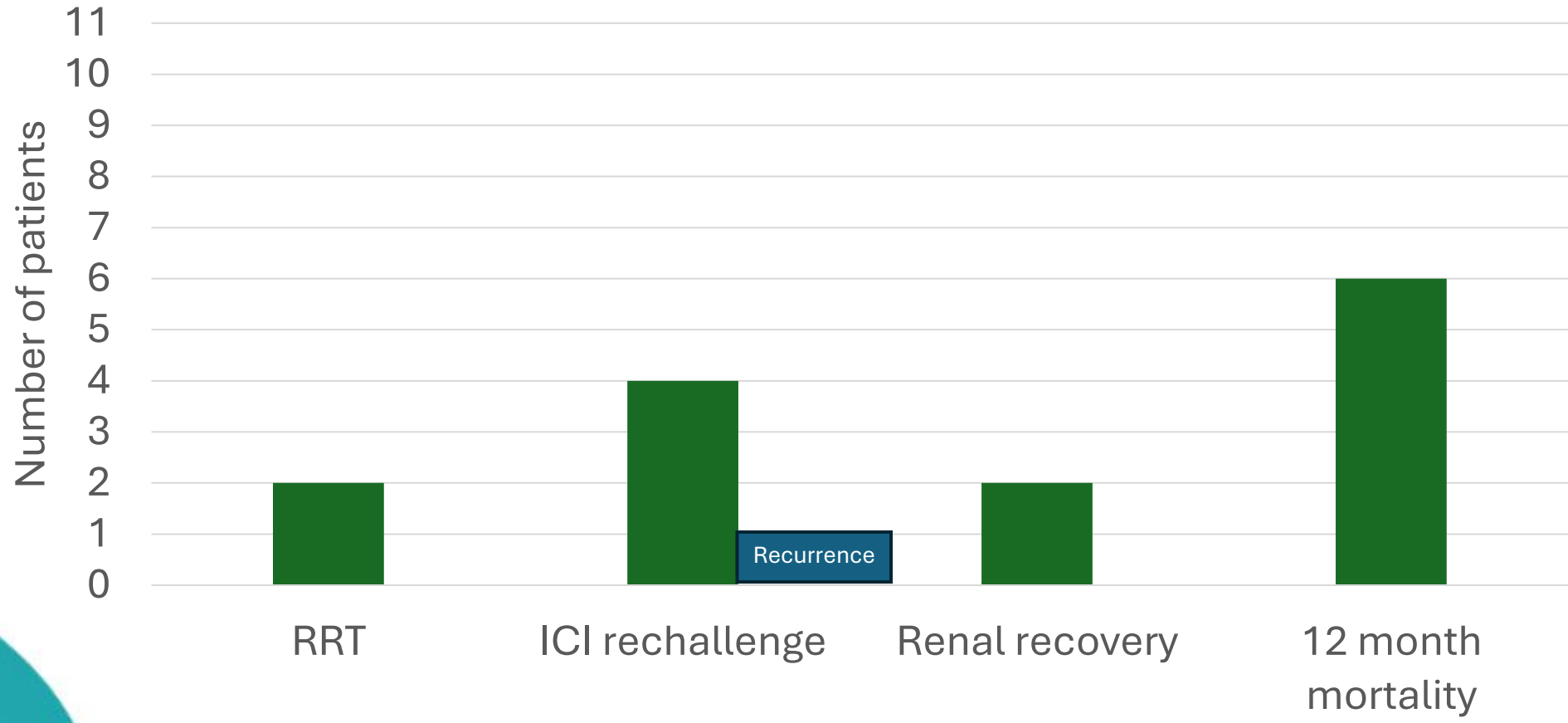
Steroids initiated: 8 (72.7%)

- IV methylprednisolone: 2 patients
- Median time to steroids: 21 days
- Median starting dose: 85 mg/day oral prednisolone (usually 1mg/kg)
- Median treatment duration with steroids (n = 5): 154 days

Second-line immunosuppression: 1 (MMF)

- Earlier treatment (within 3 days) in patients with ≥stage 2 AKI as may be associated with improved outcomes[3,4]
- Steroid dose in keeping with 2024 ASON position statement at 0.8-1mg/kg[3]
- Recommended treatment duration 6-8 weeks, with no significant difference in shorter (<28 days) vs longer duration of steroids[3,5]

ICI-AKI – Outcomes 📈



- 4 patients challenged, 1 recurrence
- Poor renal recovery at 18.2% (vs 40-87% in literature[4,6,7]). May contribute to poorer overall survival[6,9]

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Conclusion

- ICI-AKI is uncommon but significant, with poor recovery rates
- Lower baseline eGFR and ipilimumab administration are risk factors, whereas durvulumab may be safe
- Earlier recognition, biopsy, and steroid initiation is important
- Our findings contribute to the first South Australian data in this field

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