

FIGURE 10

Management of Immune-Related Renal Toxicities^{4,7,9,10,14,23,36}

Background: Renal failure related to immune checkpoint inhibitors occurs in <5% of patients. It typically presents without any clinical features at the beginning, but rising creatinine values can be detected. With progression, symptoms such as oliguria, edema, anuria and electrolyte abnormalities can occur (e.g. hyperkalemia). Median onset of immune-related events ranges from 6 to 10.5 weeks and may present months after discontinuation of therapy.

	MANAGEMENT				
	Description	Referral	Corticosteroids	Supportive Therapy	Immune Therapy
RENAL TOXICITIES	GRADE 1 Serum creatinine > ULN and 1.5-2.0 X above baseline; proteinuria 1+, <1.0g/24h.	Not required.	Not required.	Suggest hydration and cessation of nephrotoxic drugs [§] Monitor and replace fluid/electrolyte imbalances.	Monitor serum creatinine values weekly and continue immune therapy. If creatinine worsens, treat as grade 2 or 3-4.
	GRADE 2 Serum creatinine >2.0-3.0 X baseline; proteinuria 2+, 1.0-3.4g/24h.	Consider renal consultation and send urine for microscopy. Ultrasound and/or biopsy, as appropriate, to exclude non-immune causes and/or confirm immune renal toxicity.	Start prednisone 0.5-1 mg/kg daily oral or IV equivalent; once resolved to grade 0-1, taper over 2-4 weeks if 0.5 mg/kg and over 4 weeks if 1 mg/kg.	Same as above and addition of mycophenolate mofetil may be considered (has been reported in case reports in refractory cases). Hemodialysis may be required in addition to steroids if creatinine worsens (as reported in case reports).	Monitor serum creatinine q2-3 days. Withhold therapy until creatinine decreases to grade 1 & prednisone dose tapered to <10 mg/day. If creatinine increased >7days or symptoms worsen, treat as grade 3-4.
	GRADE 3 Creatinine >3.0 X baseline; proteinuria >3.5g/24h.		Start methylprednisolone 1-2 mg/kg IV daily or equivalent; taper over ≥ 4 weeks once resolved to grade 0-1.		Monitor serum creatinine daily. Permanently discontinue immune therapy.
	GRADE 4 Creatinine >6.0 X ULN. Life threatening consequences; dialysis indicated.				

§ i.e. aminoglycosides, contrast agent etc.