

**FIGURE 6**  
**Management of Immune-Related Adrenal Insufficiency**<sup>2,4,10,13,14,17,23,24,25</sup>

**Background:** Adrenal insufficiency can be classified as primary (PAI) if the adrenal glands are impaired or as secondary (SAI) if it is due to a failure of the hypothalamic-pituitary axis. Adrenal insufficiency occurs when the adrenal cortex does not produce enough cortisol (and in some cases aldosterone) and is usually characterized by hypotension, dehydration, and abnormal electrolytes, such as hyponatremia and hyperkalemia, that may mimic sepsis syndrome. Adrenal insufficiency is rare and has been reported in 0.7% of patients treated in randomized clinical trials. Adrenal insufficiency requires immediate intravenous corticosteroids after sepsis is ruled out, followed by an oral corticosteroid taper. Long-term steroid replacement is usually required. An endocrinologist should be involved and consulted as soon as adrenal insufficiency is suspected.

	Description	Referral	MANAGEMENT (First rule out infectious causes)		
			Corticosteroids	Supportive Therapy	Immune Therapy
<b>ADRENAL INSUFFICIENCY</b>	<b>GRADE 1</b> Asymptomatic or mild symptoms (fatigue); clinical or diagnostic observations only.	Consult endocrinologist. Monitor cortisol, ACTH, aldosterone and renin. Morning cortisol < 80 nmol/L strongly suggests adrenal insufficiency.	Not recommended.	Intervention not indicated.	Monitor closely and continue immune therapy.
	<b>GRADE 2</b> Moderate symptoms; medical intervention indicated.	In PAI, ACTH is high, and in SAI, ACTH is low or inappropriately normal for a low cortisol (due to pituitary impairment).	Should be initiated at 60-80 mg prednisone daily or equivalent and tapered over 1 month.	Initiate hormone replacement as needed. A medical alert bracelet/necklace is recommended.	Withhold therapy until resolution to grade 0-1. Upon improvement, treatment may be resumed after corticosteroid taper, if needed. Treatment should be continued in the presence of hormone replacement as long as no symptoms are present.
	<b>GRADE 3</b> Severe symptoms; hospitalization indicated.	As above and immediate hospitalization and management with intravenous corticosteroids after sepsis is ruled out.	Intravenous stress-dose corticosteroids (4 mg dexamethasone IV (if diagnosis unclear) or 100 mg hydrocortisone IV)*	As above and infuse 2-3 L of isotonic saline or 5% dextrose in isotonic saline as quickly as possible.	Discontinue therapy.
	<b>GRADE 4</b> Life-threatening adrenal crisis (severe hypotension or hypovolemic shock, acute abdominal pain, vomiting, and often fever); urgent intervention indicated.		Patients with primary adrenal insufficiency may also require mineralocorticoid replacement with an agent such as fludrocortisone.		

\* Hydrocortisone is recommended if confirmed PAI. Continue dexamethasone 4 mg every 12 hours and hydrocortisone 200 mg per 24 hours (via continuous infusion or q6h bolus). Taper to maintenance doses over 2 weeks post-discharge.