Immune-related Toxicity Management Pocket Guide for Physicians*

IR Toxicity	Toxicity Grade (CTCAE v5.0)	Action With ICI	Corticosteroid and/or Other Therapies
Pneumonitis	G2 (symptomatic, medical intervention indicated, limit instrumental ADL)	Withhold	• Prednisone 1-2 mg/kg equivalent followed by taper • Add prophylactic antibiotics for opportunistic infections • Gr 3/4 use methylprednisolone 1-2 mg/kg/d; add additional immunosuppressive if no improvement in 48 hr
	Recurrent G2, G3 or G4 (G3=severe symptoms, self-care ADL, O_2)	Permanently discontinue	
Diarrhea/Colitis	G2 (increase of 4-6 stools per day over baseline, moderate increase in ostomy output compared to baseline, limit instrumental ADL) or G3 (increase of 7+ stools per day over baseline, severe increase in ostomy output compared to baseline hospitalization, limit self-care ADL)	Withhold	• Prednisone 1-2 mg/kg equivalent followed by taper • GI consult and endoscopy with CT AP prior to endoscopy to rule out perforation or toxic megacolon (consider for G2, definite for G3+)
	Recurrent grade 3 or grade 4 (life-threatening consequences, urgent intervention needed)	Permanently discontinue	
AST or ALT Elevation or Increased Bilirubin	G2 AST/ALT: If baseline normal: > 3.0-5.0 x ULN; if baseline abnormal: > 3.0-5.0 x baseline bilirubin: >1.5-3.0 x ULN if baseline normal; > 1.5-3.0 x baseline if baseline abnormal	Withhold	• Administer corticosteroids (initial dose of 0.5-1 mg/kg prednisone or equivalent) followed by taper
	G3 AST/ALT: > 5.0-20.0 x ULN, if baseline normal; > 5.0-20.0 x baseline, if baseline abnormal; bilirubin: > 3.0-10.0 x ULN if baseline normal; > 3.0-10.0 x baseline if baseline abnormal G4 AST/ALT: > 20.0 x ULN, if baseline normal; > 20.0 x baseline, if baseline abnormal; bilirubin: > 10.0 x ULN if baseline normal; > 10.0 x baseline if baseline abnormal	G3: Strongly consider permanently discontinue; G4: Permanently discontinue	• Administer corticosteroids (initial dose of 1-2 mg/kg prednisone or equivalent) followed by taper
T1DM or Hyperglycemia	New onset T1DM or G3 (insulin therapy indicated, hospitalization) or G4 hyperglycemia (life-threatening consequences, urgent intervention needed) associated with evidence of β-cell failure	Withhold if DKA	• Insulin replacement if DKA (otherwise, per endocrine consult)
Hypophysitis	Grade 2 (limiting instrumental ADL)	Withhold (restart if stable)	• Administer corticosteroids and initiate hormonal replacements as clinically indicated • Monitor for hypophysitis (eg, adrenal insufficiency, hypothyroid) • Consider also checking for LH, FSH, testosterone (male), estradiol (female)
	Grade 3 or 4 G3 = hospitalization, limiting self-care ADL, not life-threatening G4 = life-threatening consequences, urgent intervention needed	Withhold or permanently discontinue (restart if ≤ G2)	

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Adrenal insufficiency	Chronic	Continue if prednisone equivalent is < 0.15 mg/kg daily	• Endocrine consult • Consider hydrocortisone ~15-30 mg total, divided as BID or TID • May need mineralocorticoid (eg, fludrocortisone) Consider androgen replacement (DHEA) • Monitor for K, BP, edema
	Adrenal crisis (usually hypotension and volume depletion)	Withhold	• Hospitalization; aggressive fluids; hydrocortisone 100 mg IV bolus, then 50 mg IV q6h
Hyperthyroidism (eg, weight loss, heat intolerance, tremor, palpitations, anxiety, increased frequency of bowel movements, and shortness of breath)	Grade 2 (symptomatic, thyroid suppression indicated, limiting instrumental ADL)	Continue	• Treat with nonselective beta-blockers (eg, propranolol) or thionamides as appropriate
	Grade 3 (severe symptoms, limiting self-care ADL, hospitalization) or G4 ((life-threatening consequences, urgent intervention needed)	Withhold or permanently discontinue (restart if ≤ G2)	
Hypothyroidism (eg, coarse hair, hair loss, decreased sweating, non-pitting edema, periorbital edema, anemia, depression, decreased hearing, diastolic hypertension, pleural and pericardial effusions, constipation, muscle cramps)	Grade 2, 3 or 4 G2 = symptomatic, thyroid replacement indicated, limiting instrumental ADL; G3 = limiting self-care ADL, hospitalization G4=(life-threatening consequences, urgent intervention needed)	Continue	• Initiate thyroid replacement hormones (eg, levothyroxine) particularly if TSH >10 or overt hypothyroidism
Nephritis (graded by Cr increase)	Grade 2 > 1.5-3.0 x baseline; > 1.5-3.0 x ULN	Withhold	• For Grade 2, prednisone 0.5-1 mg/kg/d unless persistent beyond 1 wk then increase to 1-2 mg/kg/d • Administer corticosteroids (prednisone 1 to 2 mg/kg or equivalent) followed by taper
	Grade 3 or 4 G3 = > 3.0 x baseline; > 3.0-6.0 x ULN G4 = > 6.0 x ULN	Consider permanent discontinuation	
Myocarditis	Grade 1	Withhold	• Based on severity, administer corticosteroids
	Grade 2 (symptoms with moderate activity), 3 (symptoms at rest or minimal activity, intervention indicated, or new onset of symptoms), or 4 (life-threatening consequences, urgent intervention needed)	Strongly consider permanent discontinuation for G2; Permanently discontinue for G3+	
Mucocutaneous	G1-2	Continue	• Topical corticosteroids, emollients, and oral
	G3-4 (eg, macules/papules covering > 30% body surface area with moderate or severe symptoms; limiting self-care ADL)	Withhold	• Prednisone 0.5-1 mg/kg/d equivalent, tapered over 2-4 wks; high potency topical steroid

References:

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*This guide has been developed to accompany the CE activity titled, Optimizing the Management of Advanced Gastric Cancer: The Importance of Knowing When and How to Utilize Immune Checkpoint Inhibitors, on PowerPak at https://www.powerpak.com/course/preamble/123182 and Medscape, September 2022. It is not intended as a standalone reference.

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