Improving outcomes of immune-related adverse events: The crucial role of the pharmacist

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Expert panel

Dr Sandra Cuellar

University of Illinois,
Chicago, USA

Dr Sonia Amin Thomas

Wellstar North Fulton Hospital and
Northwest Georgia Oncology Center,
Roswell, GA, USA

Ms Meera Desai

University College London
Hospitals NHS Foundation Trust,
London, UK

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Agenda

- Key considerations for identifying and monitoring irAEs
- Approaches to recognizing and managing irAEs
- Building strategies for monitoring and management of irAEs

irAE, immune-related adverse event.

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Key considerations for identifying and monitoring irAEs

Dr Sandra Cuellar

University of Illinois,
Chicago, USA

irAE, immune-related adverse event.

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Commonly observed irAEs (1/2)

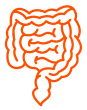
Cutaneous irAEs

- Inflammatory dermatoses
- Bullous dermatoses
- Severe cutaneous adverse reactions

Most common irAE

≤72% of patients

Median time to onset
3–6 weeks
after therapy initiation



Gastrointestinal irAEs

- Colitis
- Hepatitis
- Gastritis
- Enterocolitis
- Lower GI toxicities more common

Colitis: 8–27% of patients*
Diarrhoea: ≤54% of patients*

Median time to onset
6 weeks
after therapy initiation

Endocrine irAEs

- Characterized by the gland or organ affected

Clinically significant endocrinopathy

10% of patients

Median time to onset
14.5 weeks
after therapy initiation

Respiratory irAEs

- Pneumonitis

Uncommon but potentially serious

10% of patients*

Median time to onset
34 weeks
after therapy initiation

*In patients treated with combination therapy.
GI, gastrointestinal; irAE, immune-related adverse event.
Schneider BJ, et al. *J Clin Oncol*. 2021;9:4073–126.

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Commonly observed irAEs (2/2)

Haematologic irAEs

- Haemolytic anaemia
- Acquired TTP
- Haemolytic uraemic syndrome
- Aplastic anaemia
- Lymphopenia
- Immune thrombocytopenia
- Acquired haemophilia A

Haemolytic anaemia:
10% of patients

Median time to onset
5.7 weeks
after therapy initiation

Renal irAEs

- Nephritis
- Acute kidney injury

4.5% of patients*

Median time to onset
14 weeks
after therapy initiation

Neurologic irAEs

- Myasthenia gravis or myasthenic syndrome
- Aseptic meningitis
- Encephalitis
- Guillain–Barré-like syndrome
- Variety of other peripheral neuropathy phenotypes and demyelinating disorders

12% of patients*

Median time to onset
4 weeks
after therapy initiation

Cardiovascular irAEs

- Myocarditis
- Pericarditis
- Arrhythmias
- Impaired ventricular function with heart failure
- Vasculitis
- Venous thromboembolism

High mortality risk

<0.3% of patients*

Median time to onset
6 weeks
after therapy initiation

*In patients receiving combination therapy.
irAE, immune-related adverse event; TTP, thrombotic thrombocytopenic purpura.
Schneider BJ, et al. *J Clin Oncol*. 2021;9:4073–126.

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Approaches to recognizing and managing irAEs

Dr Sandra Cuellar

University of Illinois
Chicago, USA

irAE, immune-related adverse event.

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The challenges to early recognition of irAEs

- Non-specific early symptoms, e.g. dyspnoea and fatigue
- Different safety profiles and irAE presentations
- Difficult to distinguish irAEs in patients receiving combination therapies, e.g. ICI plus chemotherapy

- Delayed time to onset: up to 1 year after ICI therapy completion or discontinuation
- Delayed patient reporting, e.g. poor awareness of symptoms, limited access to emergency care

- Limited monitoring strategies between treatment cycles
- Lack of cost-effective monitoring strategies for rare but life-threatening irAEs
- Lack of non-invasive diagnostic procedures

ICI, immune checkpoint inhibitor; irAE, immune-related adverse event.

Medina P, et al. *J Pharm Pract*. 2020;33:338–49.

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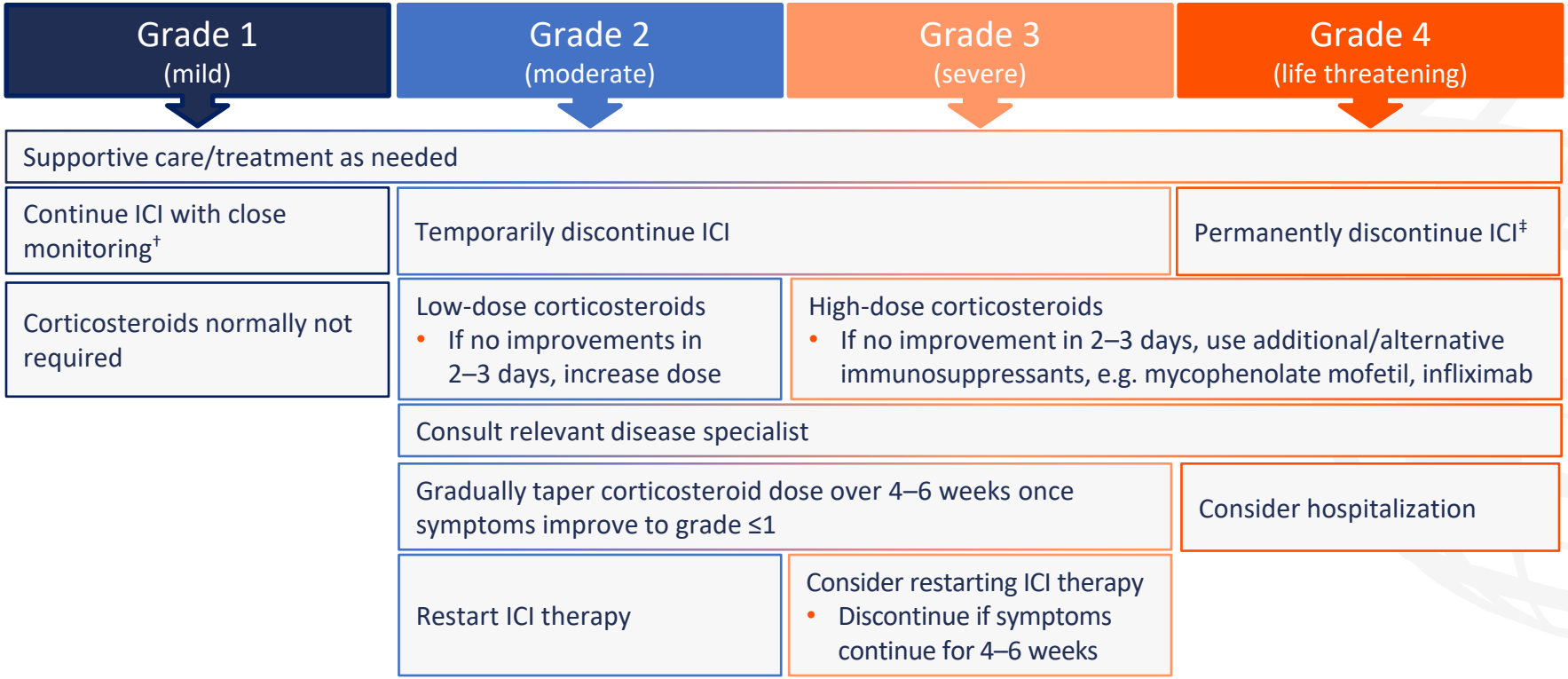
Overall summary of irAE management strategies*



*Guidelines for treatment recommendations for each specific irAE should be consulted; †For some neurologic, haematologic or cardiac irAEs, ICI therapy should be discontinued at any grade until the nature of the irAE is defined; ‡Therapy with ICI can continue if grade 4 irAE is an endocrinopathy which can be controlled with hormone replacement. ICI, immune checkpoint inhibitor; irAE, immune-related adverse event.

Medina P, et al. *J Pharm Pract*. 2020;33:338–49.

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Building strategies for monitoring and management of irAEs

Dr Sandra Cuellar

University of Illinois
Chicago, USA

irAE, immune-related adverse event.

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The core pillars for irAE management[1,2]

Prevent	• Know the irAE spectrum – keep potential irAEs in mind and consider the median time to onset • Identify the risk factors – review past medical history and identify patients at high risk of irAEs • Educate patients and caregivers to identify signs and symptoms of irAEs
Anticipate	• Assess patients • Review lab results regularly and prior to each treatment cycle • Assess toxicities during phone and follow-up appointments
Detect	• Maintain a high index of suspicion and be aware of treatment history in case of delayed-onset irAEs • Encourage patients to report symptoms • Look for changes in baseline values • Distinguish irAEs from other AEs related to other therapies, and eliminate disease progression
Treat	• Individualize immunosuppression treatment plan • Design appropriate steroid taper schedule • Discuss immunotherapy suspension and refer to organ specialist • Educate patients and team on potential consequences of treatment
Monitor	• Monitor for irAE relapse or recurrence during steroid taper • Recommend prophylaxis if needed • Monitor for complications of ICI therapy and immunosuppressive agents

AE, adverse event; ICI, immune checkpoint inhibitor; irAE, immune-related AE.

1. Medina P, et al. *J Pharm Pract*. 2020;33:338–49; 2. Champiat S, et al. *Ann Oncol*. 2016;27:559–74.

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