Update in Internal Medicine 2026

Saturday, May 2 • 8 a.m. – 4 p.m.

UT Southwestern Medical Center, T. Boone Pickens Medical Education & Conference Center

Complications of cancer immunotherapy

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Disclosures

- No relevant financial disclosures

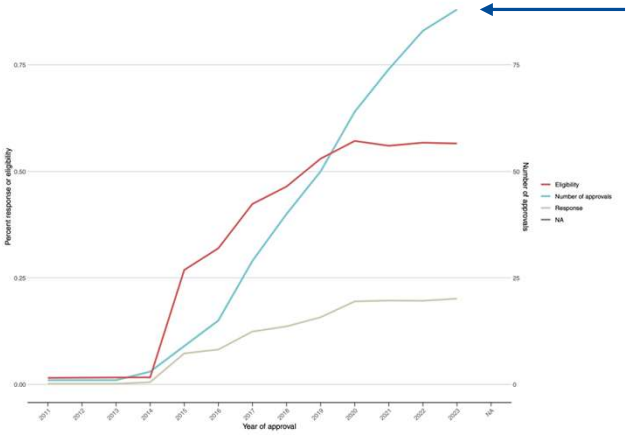
Learning Objectives

- Recognize common and serious cancer immunotherapy toxicity by organ system
- Describe first-line and adjuvant management
- Distinguish ICI toxicity from CAR-T/BiTE toxicity

Cancer immunotherapy has revolutionized modern oncology practice

Why this matters

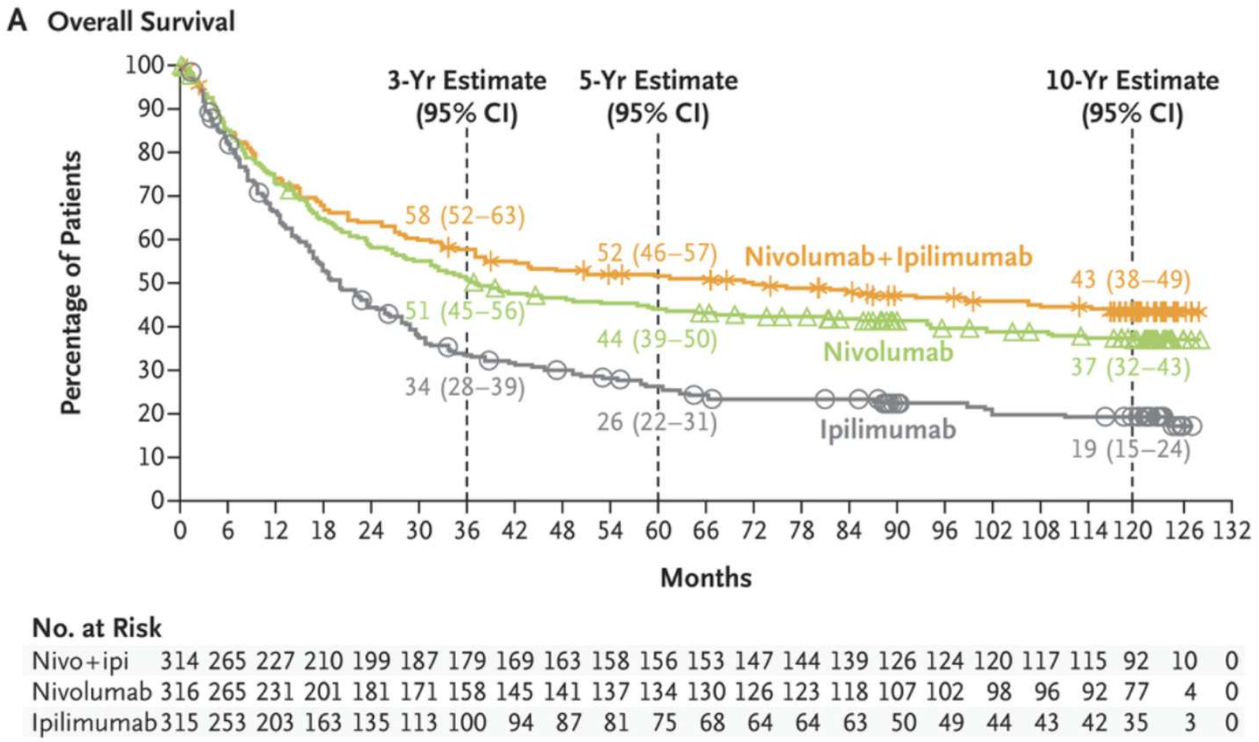
- Immunotherapy is a standard treatment for most advanced cancers
- Hundreds of thousands of patients in the US annually
- Toxicity is common and can be difficult to diagnose and treat



Haslam *et al*, Int J Cancer, 2025. Haslam *et al*, Blood Adv, 2024.

Dramatic survival gains

Median survival >5 years



Median survival <6 months

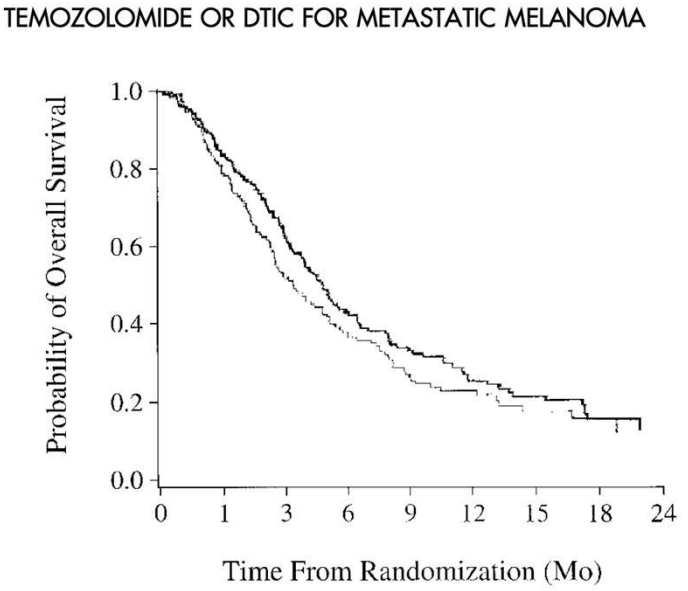


Fig 1. Overall survival in the temozolomide (thick line) and DTIC (thin line) treatment groups.

Wolchok *et al*, NEJM, 2024.

Middleton *et al*, J Clin Oncol, 2000.

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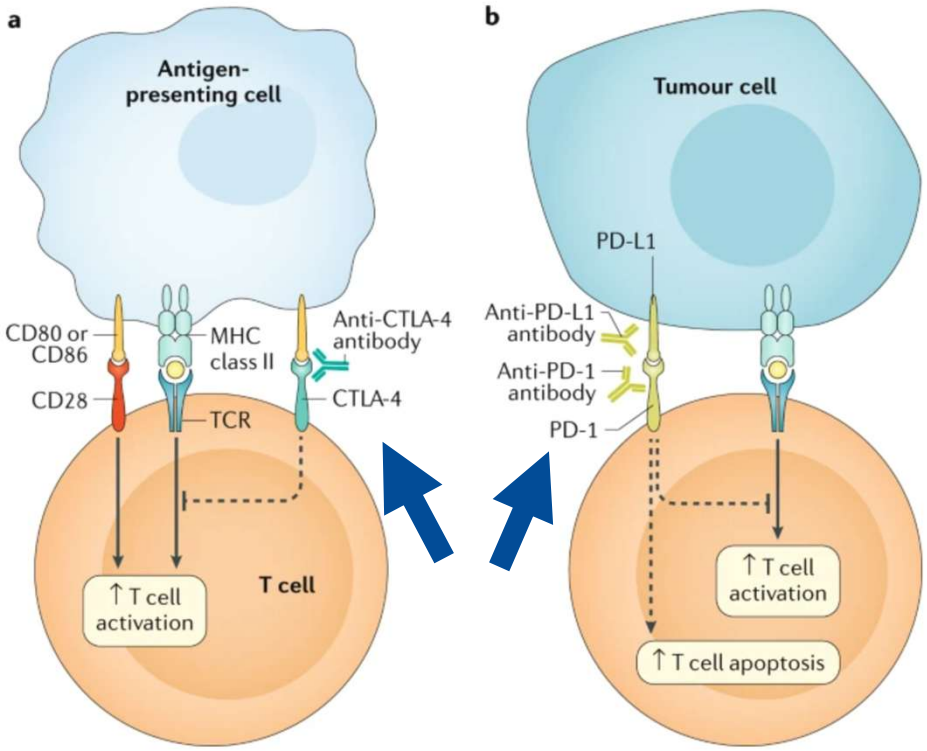
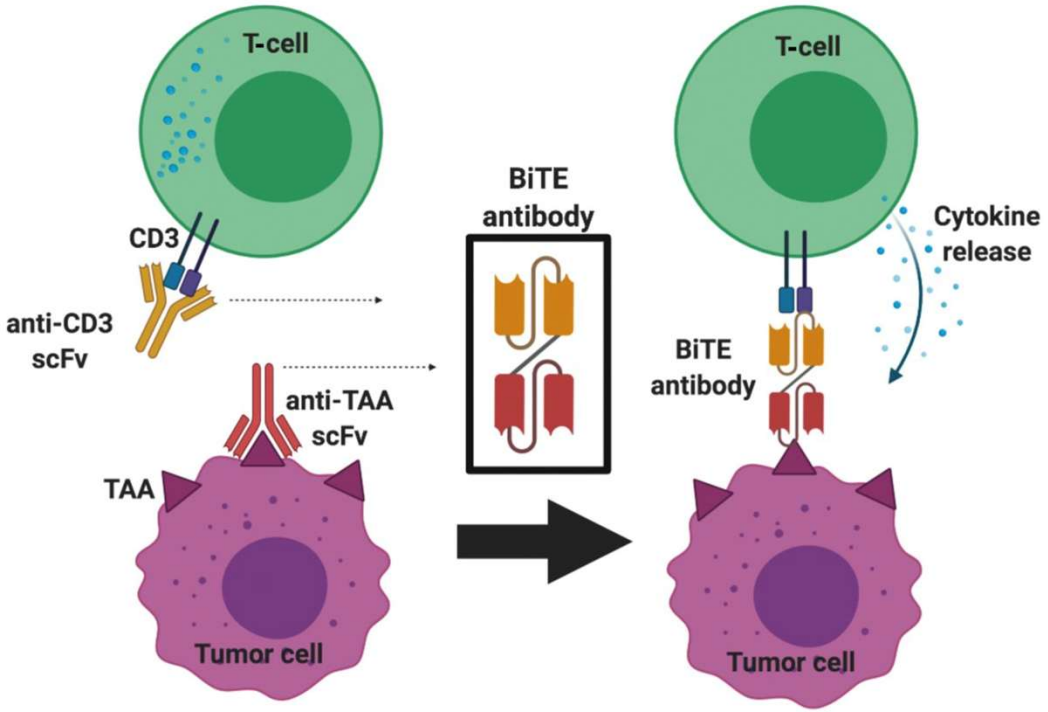
Categories of immunotherapy - ICI



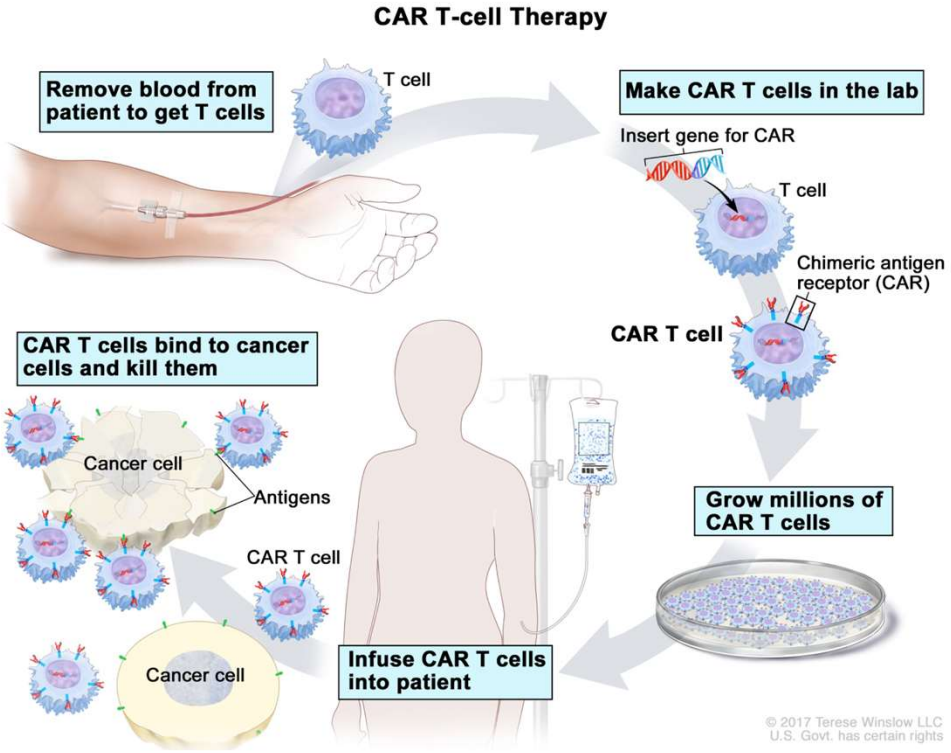
Ramos-Casals *et al*, Nat Rev Dis Primers, 2020.

Categories of immunotherapy

BiTE



CAR-T

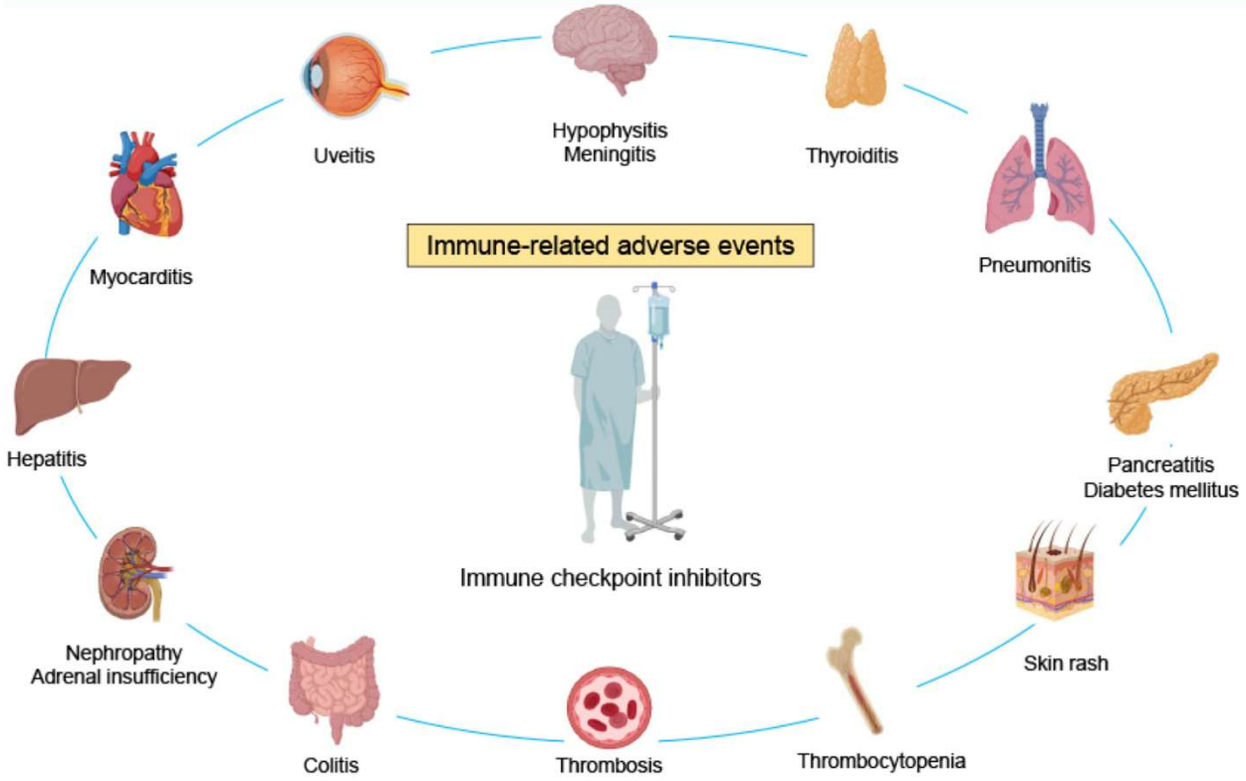


Rallis *et al*, Anticancer Res, 2021.

National Cancer Institute, accessed online March 2026
https://www.cancer.gov/publications/dictionaries/cancer-terms/def/car-t-cell-therapy

ICI toxicities are common and unpredictable

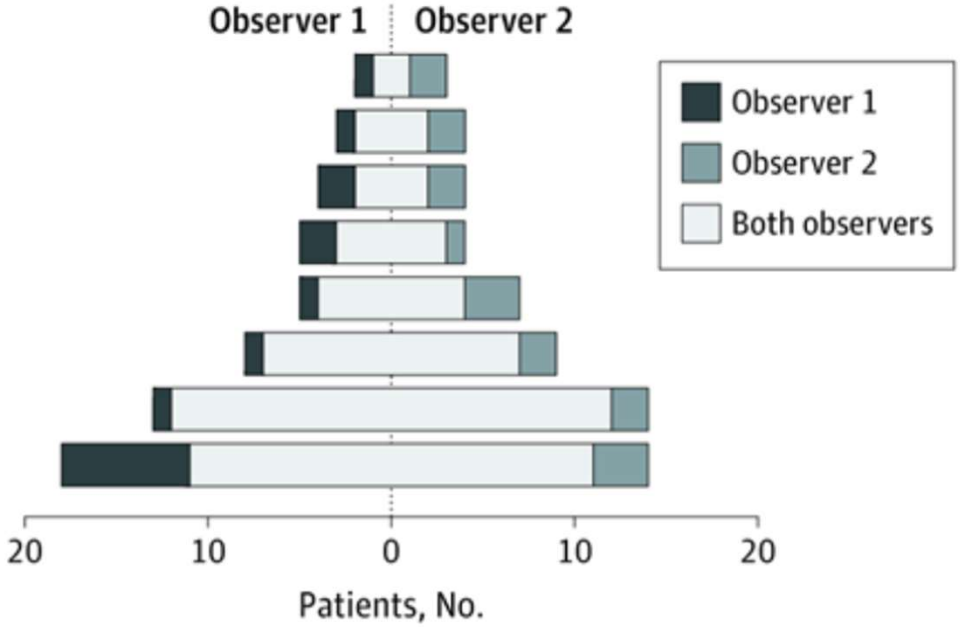
ICI toxicities are known as immune-related adverse events (irAE)



Dang *et al*, Int J Mol Sci, 2023.

irAE are difficult to diagnose

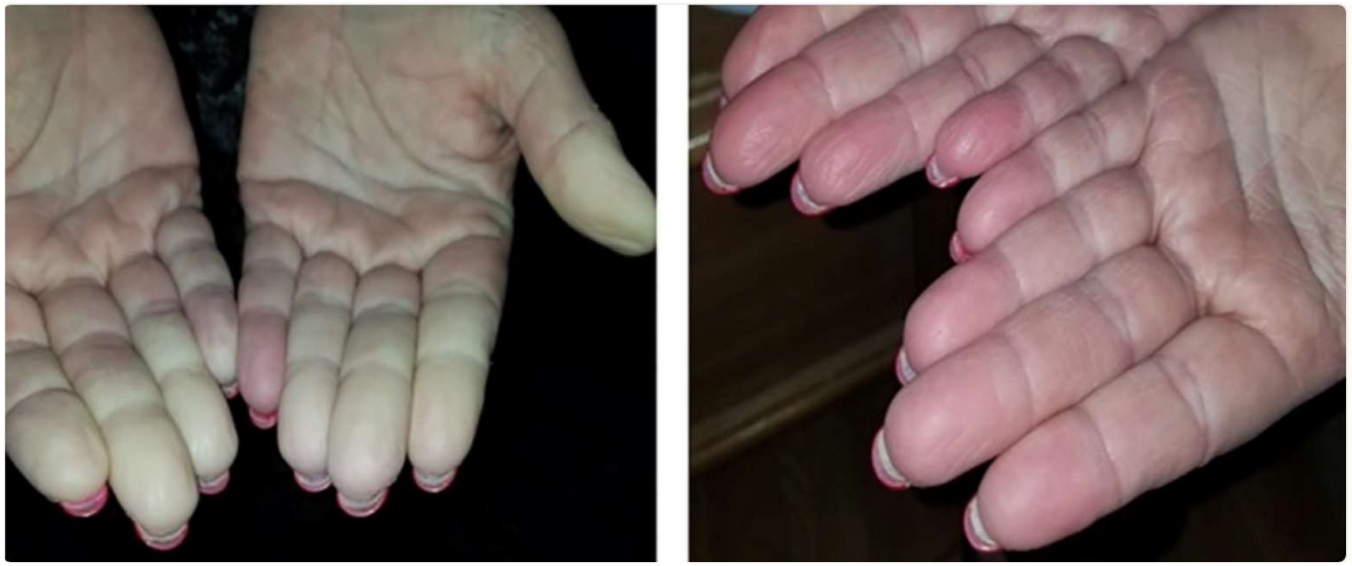
irAE	Cohen κ	Weighted κ
Hypophysitis	0.37	0.31
Hyperthyroidism	0.64	0.57
Adrenal insufficiency	0.46	0.40
Rash	0.64	0.64
Colitis	0.62	0.68
Hepatitis	0.63	0.59
Hypothyroidism	0.80	0.75
Pneumonitis	0.55	0.58



- Most irAEs have only moderate inter-rater agreement (κ <0.65), highlighting diagnostic uncertainty

Hsiehchen *et al*, JAMA Netw Open, 2019.

Can occur late and even after stopping treatment



Raynaud's onset 2 years after starting ICI

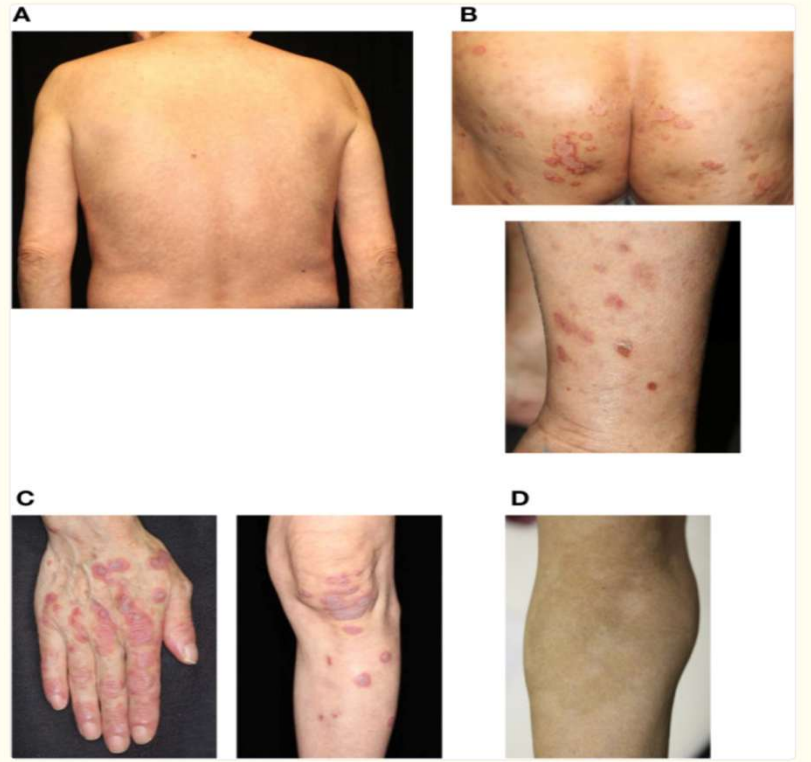
Khan *et al*, Oncologist, 2020.

Approach to suspected irAE presentation

- Step 1: Rule out infection / progression
- Step 2: Grade toxicity (CTCAE or ASCO/SITC guidelines)
- Step 3: Grade 1 → continue ICI
  Grade 2 → hold + prednisone 0.5–1 mg/kg
  Grade ≥3 → higher-dose steroids + consult + admit
- Step 4: Steroid taper ≥4-6 weeks – (consider PPI and Bactrim)

Dermatitis

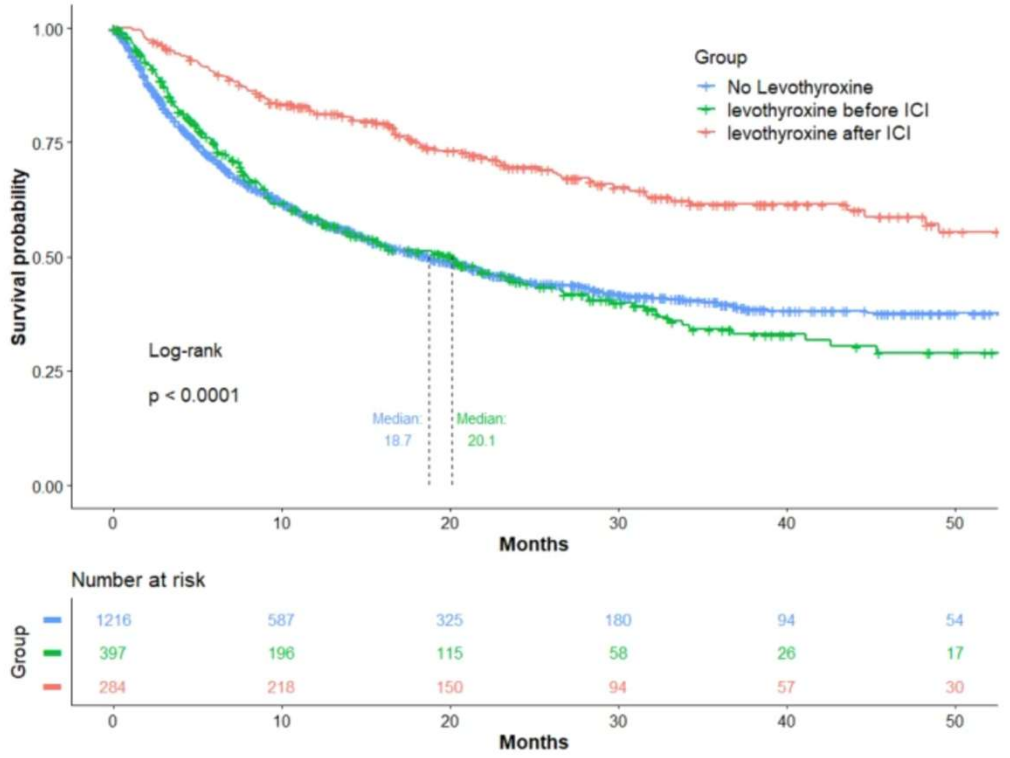
- ~30-50% incidence
- Commonly maculopapular rash and/or pruritus
- Can respond well to topical steroids and antihistamines
- Rarely causes SJS/TEN



Watanabe *et al*, Front Immunol, 2023.

Thyroiditis

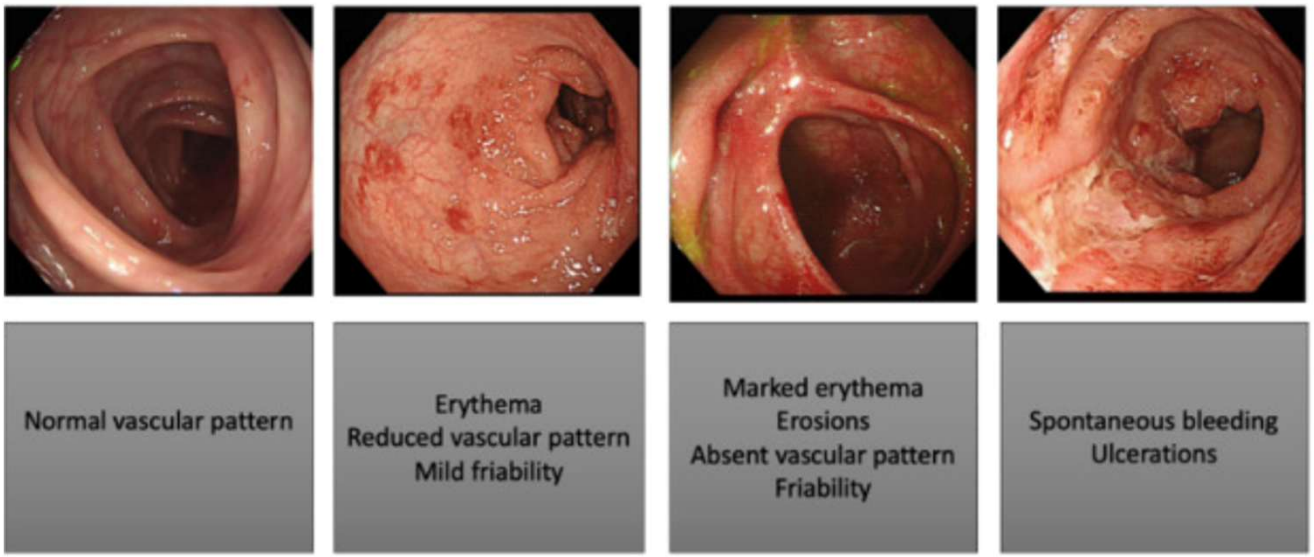
- ~20% incidence
- Initially hyper, then hypothyroidism
- Requires hormone replacement
- Not treated with immunosuppression



von Itzstein *et al*, Cancer Immunol Immunother, 2022.

Colitis

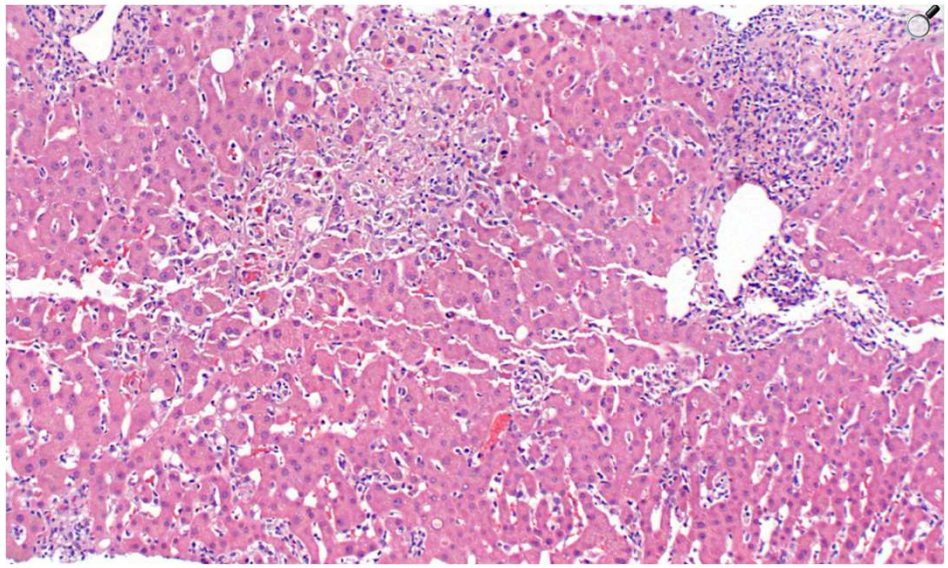
- ~10-20% incidence, can require hospitalization
- Workup requires infectious rule out
- Colonoscopy with biopsy can be helpful to confirm diagnosis



Mok *et al*, Clin Col Cancer, 2024.

Hepatitis

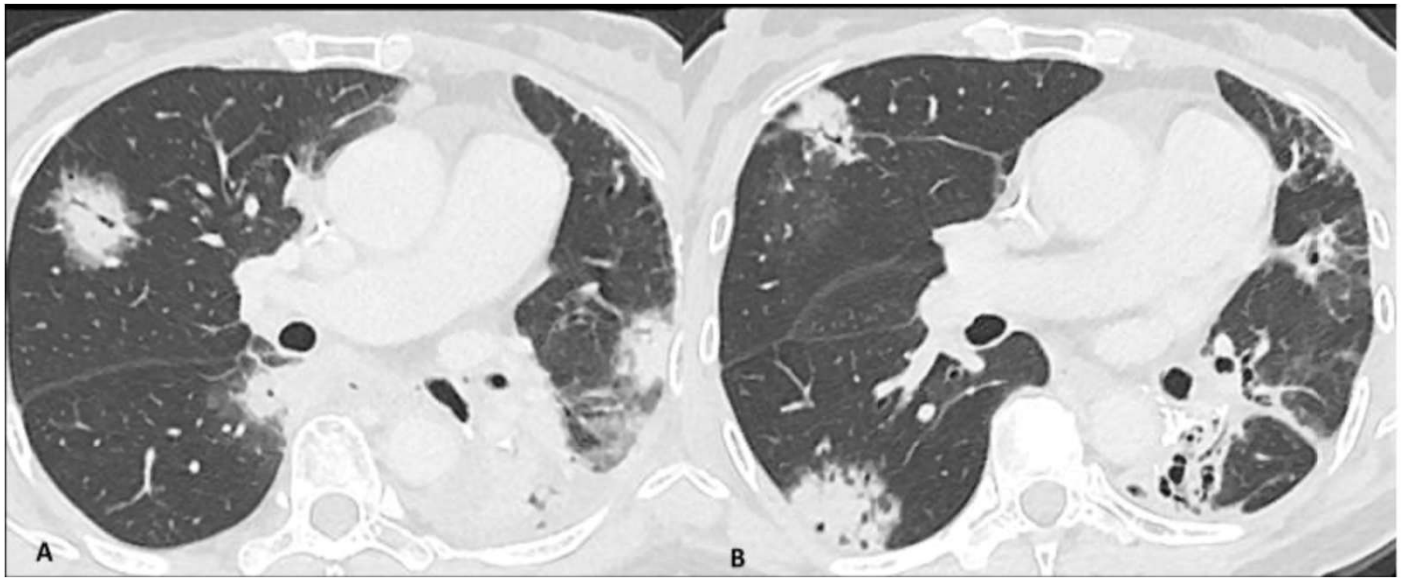
- ~10% incidence
- Can require hospitalization
- Infliximab generally avoided, MMF preferred if steroids not sufficient



Cohen *et al*, Mod Pathol, 2021.

Pneumonitis

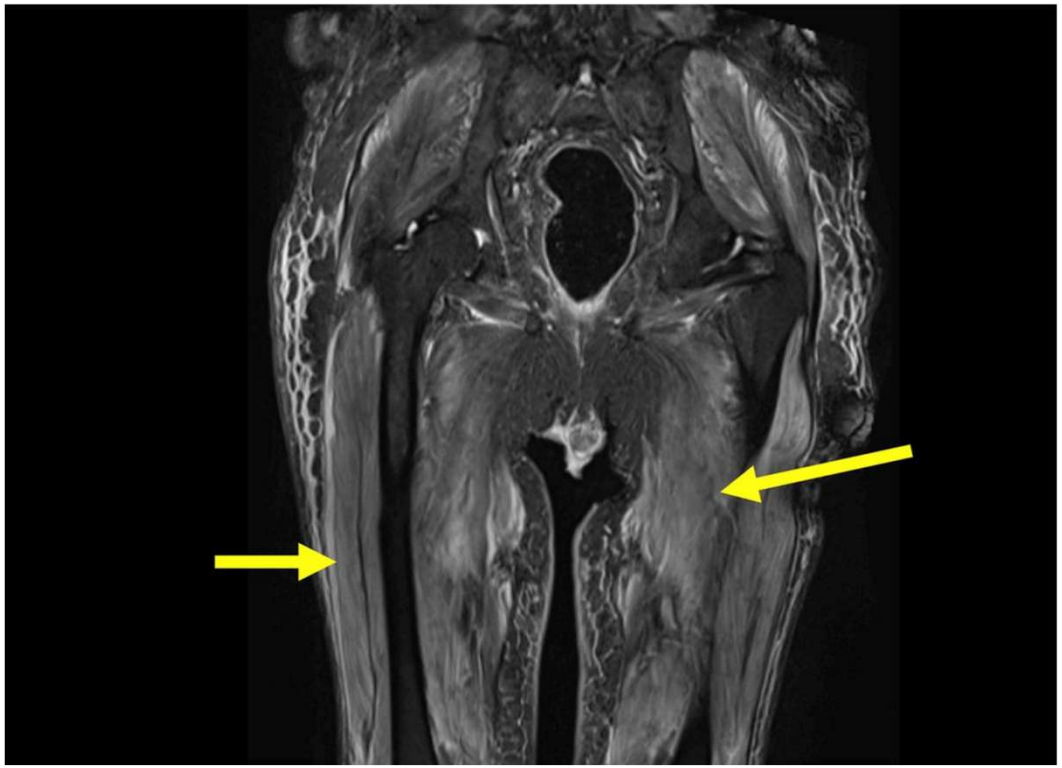
- ~5-10% incidence
- Commonly requires hospitalization
- Variable radiographic appearance
- Diagnostic challenge in lung cancer patients with COPD and radiation history



Pozzessere *et al*, Cancers, 2024.

Arthritis/Myositis

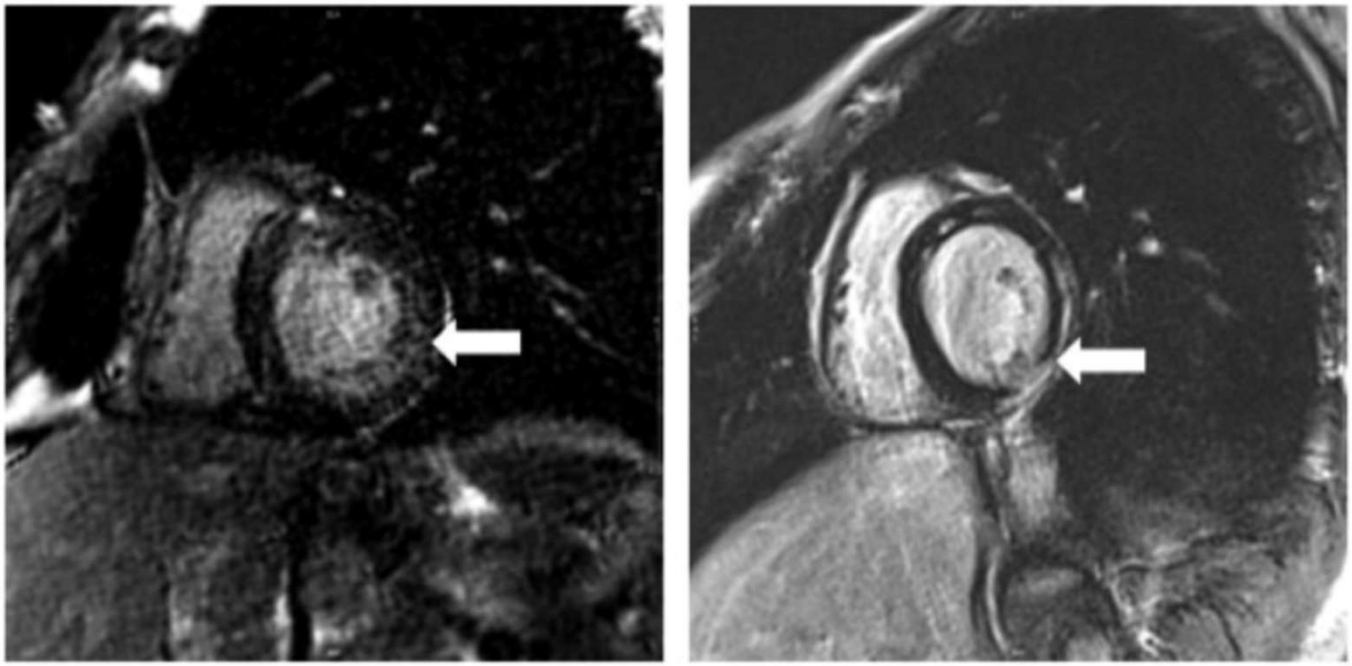
- Myositis often proximal and can be misinterpreted as liver injury based on AST/ALT elevation
- Arthritis often chronic and benefits from rheumatology management



Agarwal *et al*, BMJ Case Rep, 2025.

Myocarditis

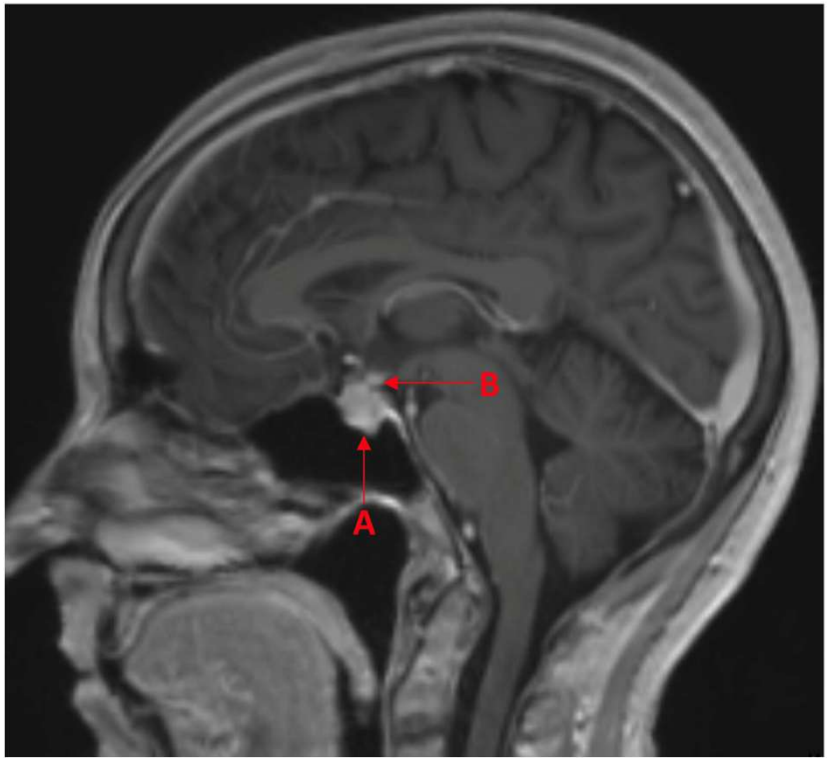
- Rare but more common with combination ICI - up to 1-2%
- High fatality rate, needs urgent cardiology involvement
- Myasthenia/myositis overlap



Zhang *et al*, Eur Heart J, 2020.

Hypophysitis

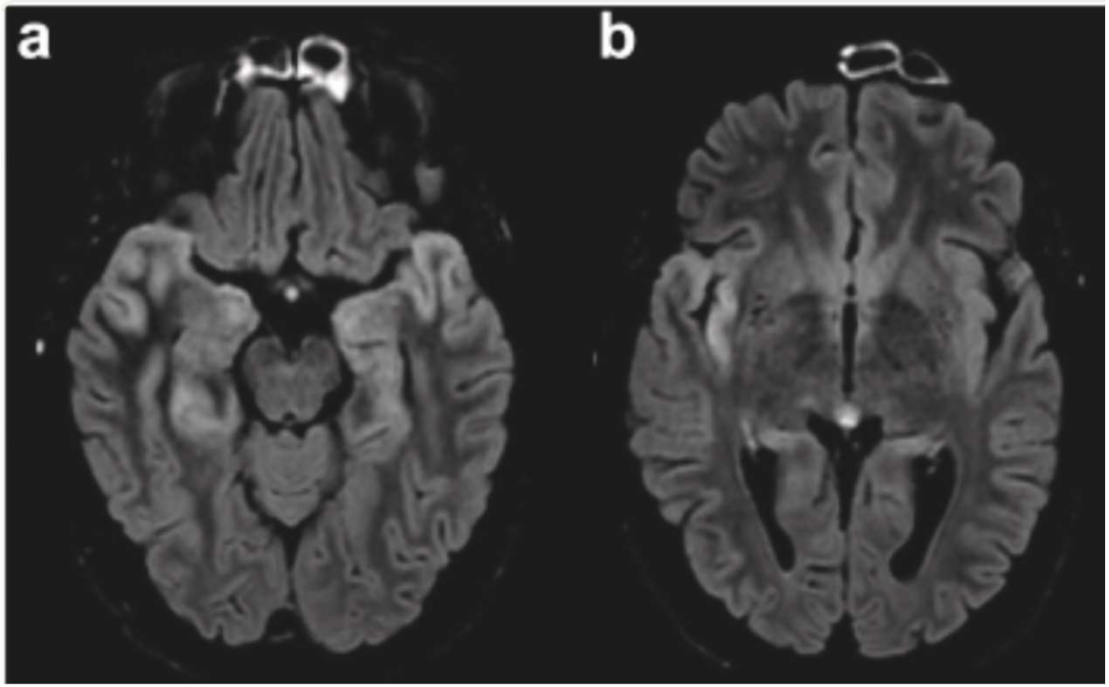
- Primarily seen with CTLA-4 use in up to 5-10%
- Most commonly central adrenal insufficiency



Qi *et al*, Clin Endocrinol, 2025.

Encephalitis

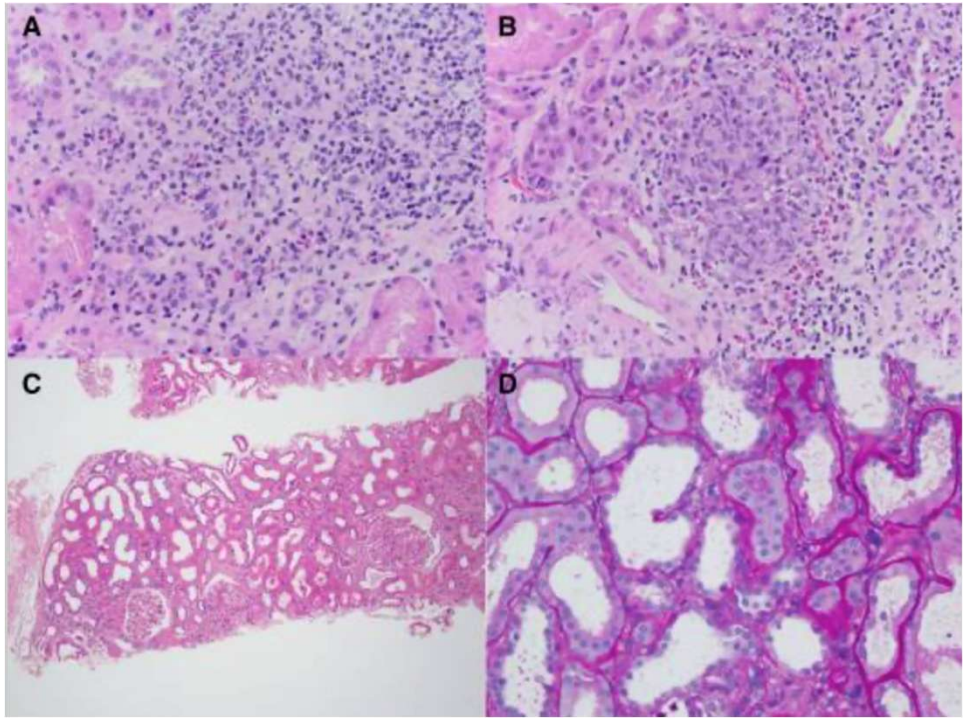
- Rare (<1%) but can be fatal
- Requires hospitalization and early neurology consultation
- Differential is metastases or infection, MRI and lumbar puncture needed



Farina *et al*, Lancet Reg Health Eur, 2024.

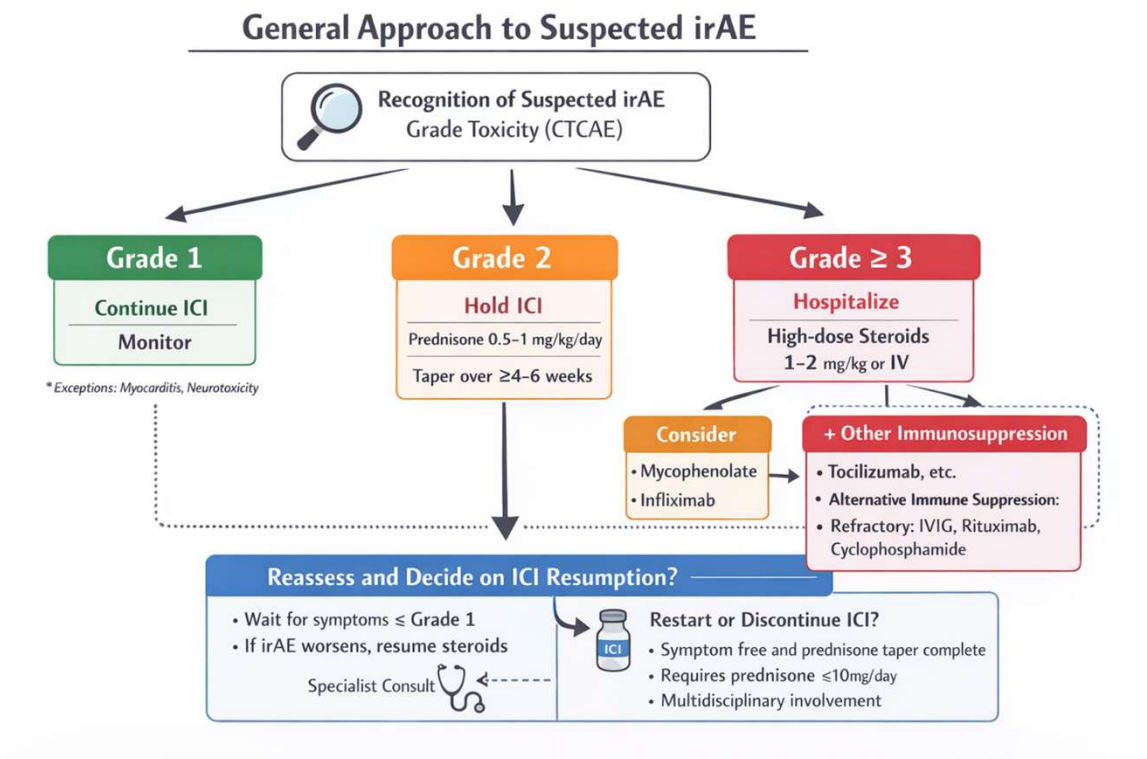
Nephritis

- Rare ~1-2% but can result in need for permanent dialysis
- Wide differential for elevated creatinine and hypovolemia, infection, or other drug toxicity is more common
- Kidney biopsy to confirm



Rashidi *et al*, Kidney360, 2022.

Workup and management overview



Adapted from Tian *et al*, Cancer Biol Med, 2025.

Additional immunosuppression pearls

- ICI-colitis: αβ integrin inhibitor **vedolizumab**
- ICI-myocarditis: CD80/CD86-CD28 inhibitor **abatacept**
- Common adjuvant immunosuppression options include mycophenolate mofetil (**MMF**), **infliximab**, **tocilizumab**

Timing Patterns

- Any irAE can occur at any timepoint – **vigilance**
- Early (weeks) – dermatitis, myocarditis, colitis
- Medium (months) – pneumonitis, hepatitis
- Late – thyroiditis, arthritis/myositis, nephritis

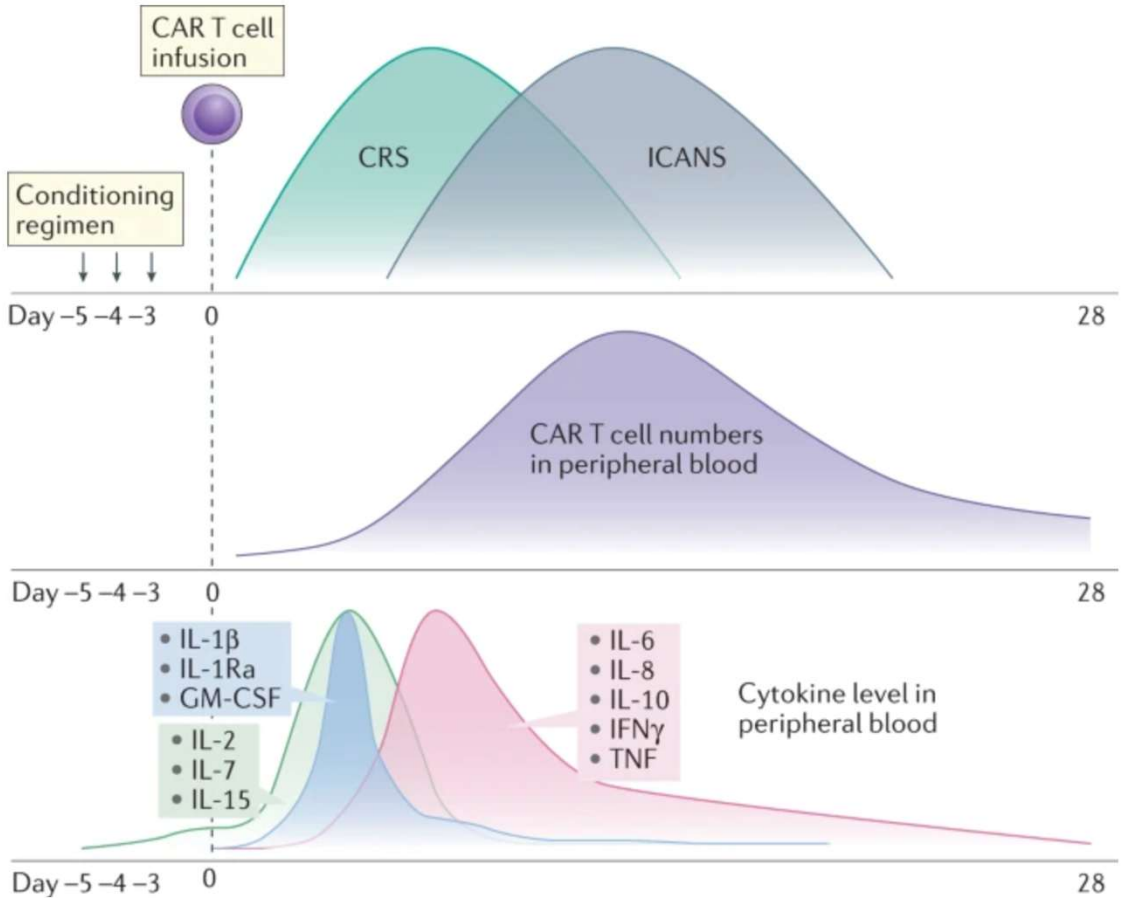
Connolly *et al*, Front Oncol, 2019.

CAR-T and BiTE toxicities are common, but in contrast to ICI toxicity, are predictable

CAR-T and BiTE Toxicity

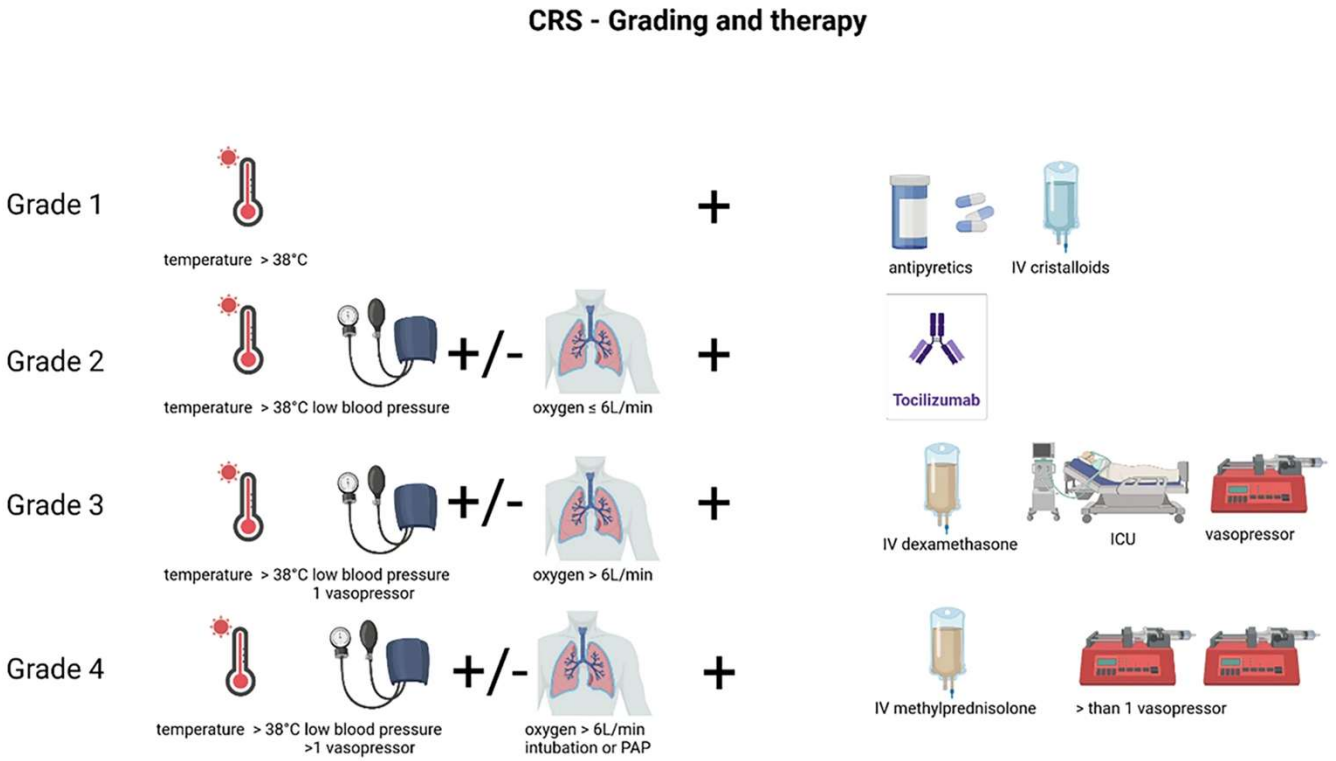
- Cytokine release syndrome (CRS) – hours to days
- Immune effector cell-associated neurotoxicity syndrome (ICANS) – days to weeks

Fig. 1: Schematic diagram showing a relative timescale for the onset and duration of CRS and ICANS.



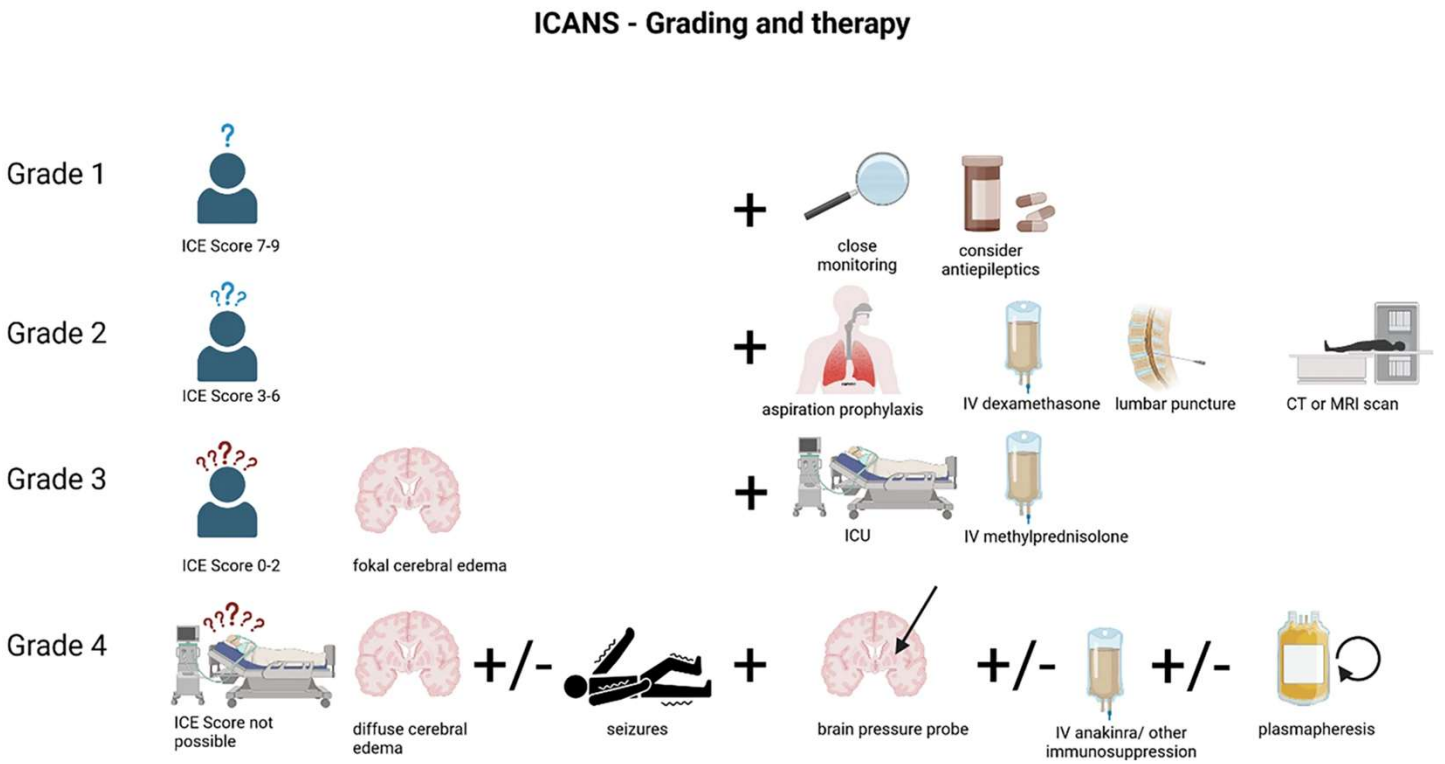
Morris *et al*, Nat Rev Immunol, 2022.

CAR-T and BiTE CRS Management



Schroeder *et al*, Intensive Care Med, 2024.

CAR-T and BiTE ICANS Management



Schroeder *et al*, Intensive Care Med, 2024.

Take Home Messages

- ICI toxicity = autoimmune, multisystem
- Can occur any time (even years later)
- Steroids are cornerstone, adjuvant immunosuppression may be needed
- CAR-T/BiTE = cytokine-driven syndromes, more predictable
- **Early recognition saves lives – be vigilant**