sitc Society for Immunotherapy of Cancer

ADVANCES IN Cancer IMMUNOTHERAPY™

Toxicity Management

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AAEM AMERICAN ACADEMY OF EMERGENCY MEDICINE CHAMPION OF THE EMERGENCY PHYSICIAN

ACCC Association of Community Cancer Centers

HOPA Hematology/Oncology Pharmacy Association

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Disclosures

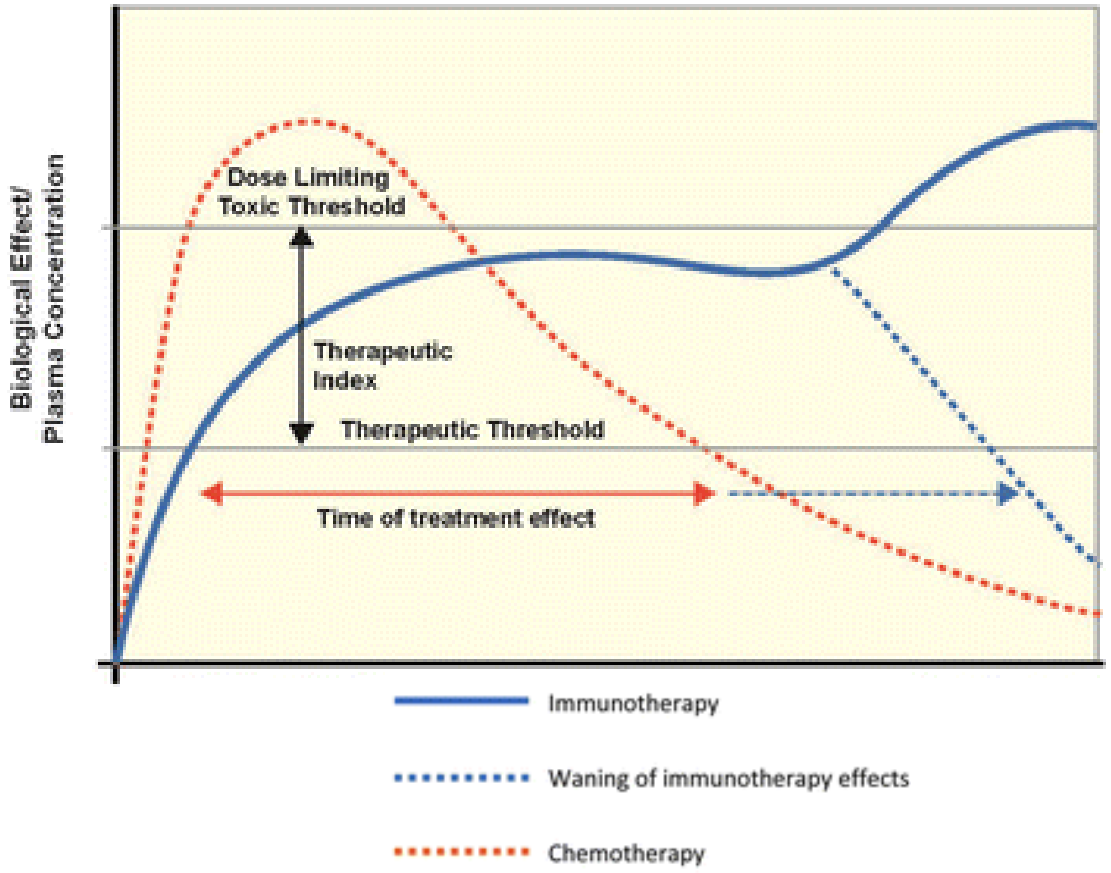
- I have nothing to disclose.
- I will be discussing non-FDA approved indications during my presentation.

Outline

- Incidence, onset and severity grading
- Immune checkpoint inhibitors
  - Common adverse events
  - Rare but serious adverse events
  - Impact of irAEs on cancer outcomes
- Cellular therapies
  - Adverse events and management
- Immunotherapy in special patient populations
- Case studies

Immune-Related Adverse Events (irAEs)

- Immune checkpoint inhibitor (ICI) toxicities often have delayed onset and prolonged duration relative to cytotoxic chemotherapy
- Toxicities result from activation of the immune response, and can mimic a number of autoimmune medical conditions



Puzanov and Diab, JITC 2017

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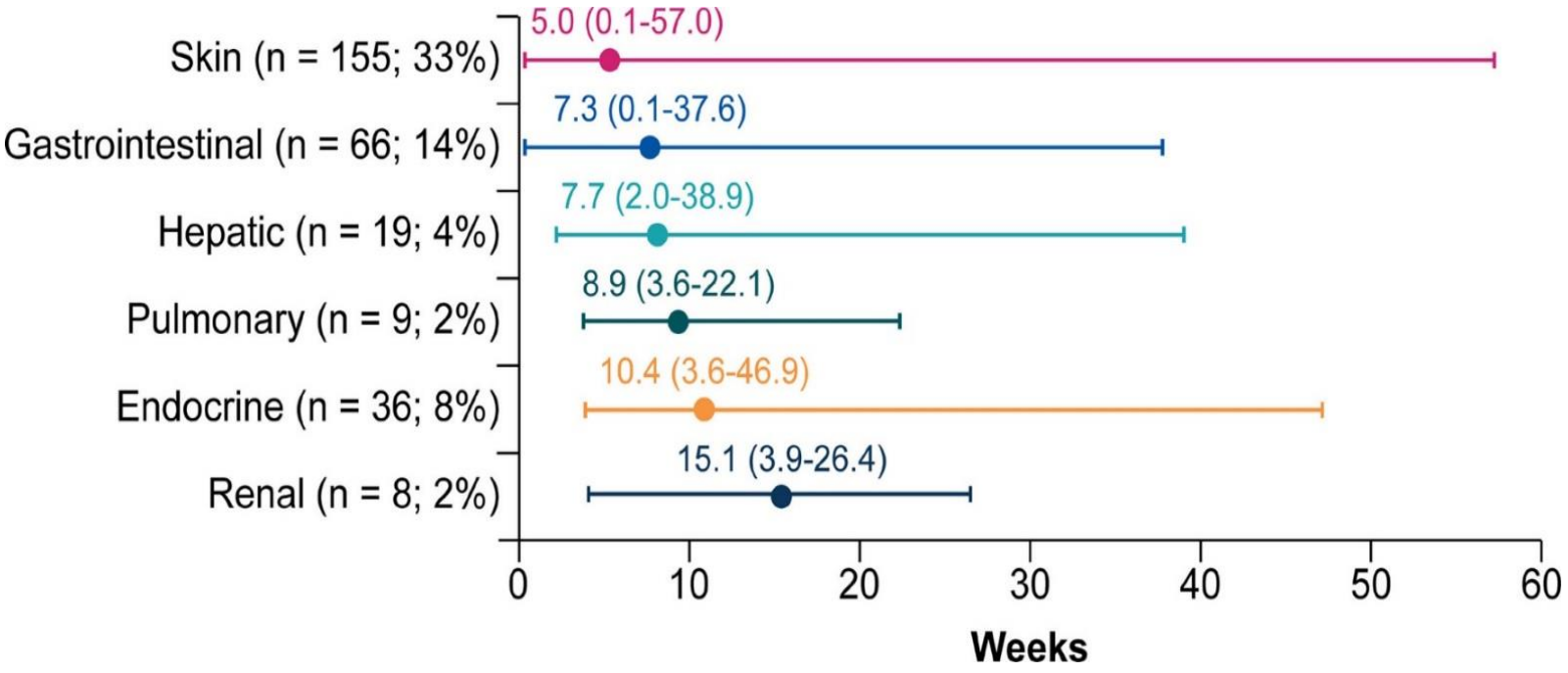
Onset of irAEs



- Can be days to months after therapy initiation
- May occur even after treatment is discontinued
- Onset may be earlier with combination treatments
- Important to identify patients who are currently **OR** previously on ICI treatment!

Pallin, Acad Emerg Med 2018
Puzanov and Diab, JITC 2017

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Common Terminology Criteria for Adverse Events (CTCAE)

CTCAE Grade	Clinical description
1	Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated
2	Moderate; minimal, local, or noninvasive intervention indicated; limiting age-appropriate instrumental ADL
3	Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self care ADL
4	Life-threatening consequences; urgent intervention indicated
5	Death related to adverse event

US Dept of HHS, 2017.

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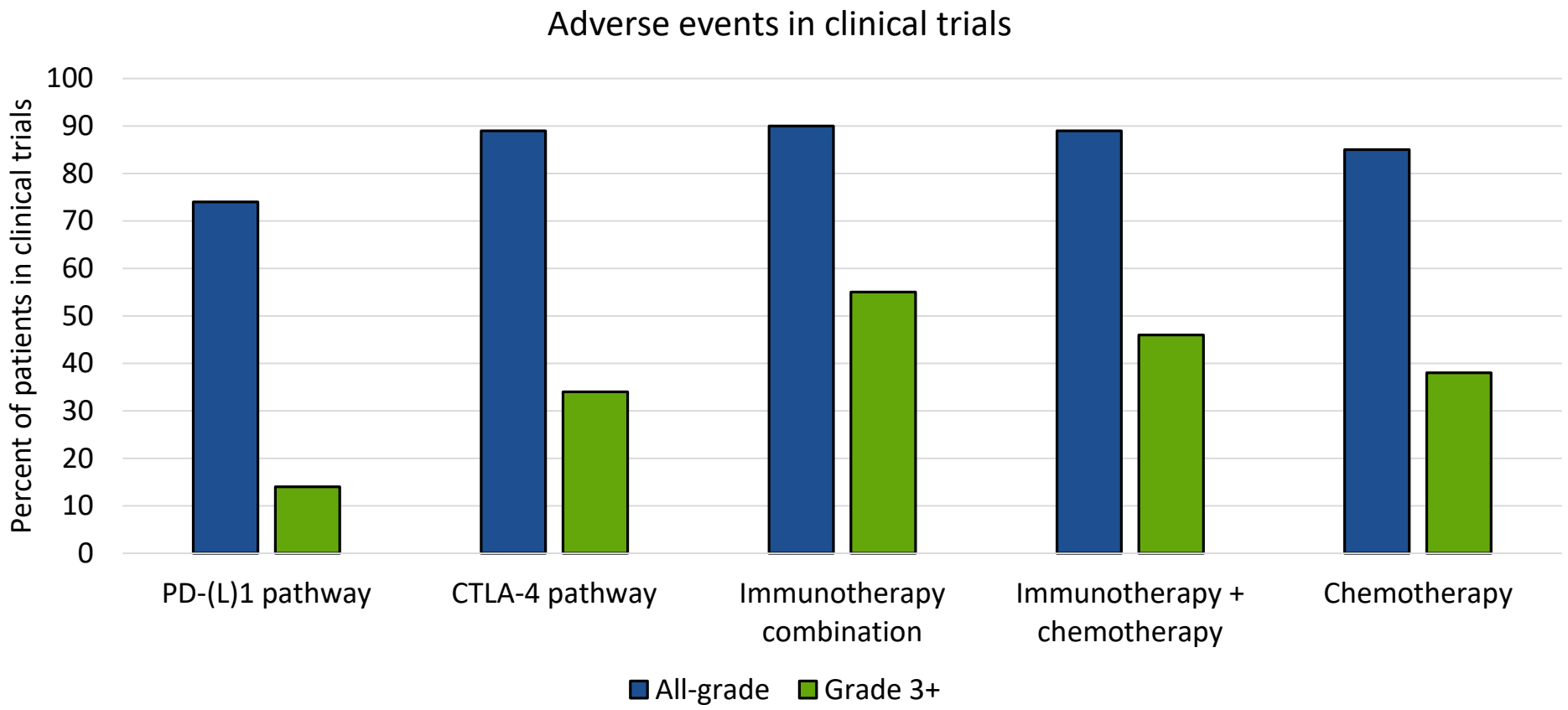
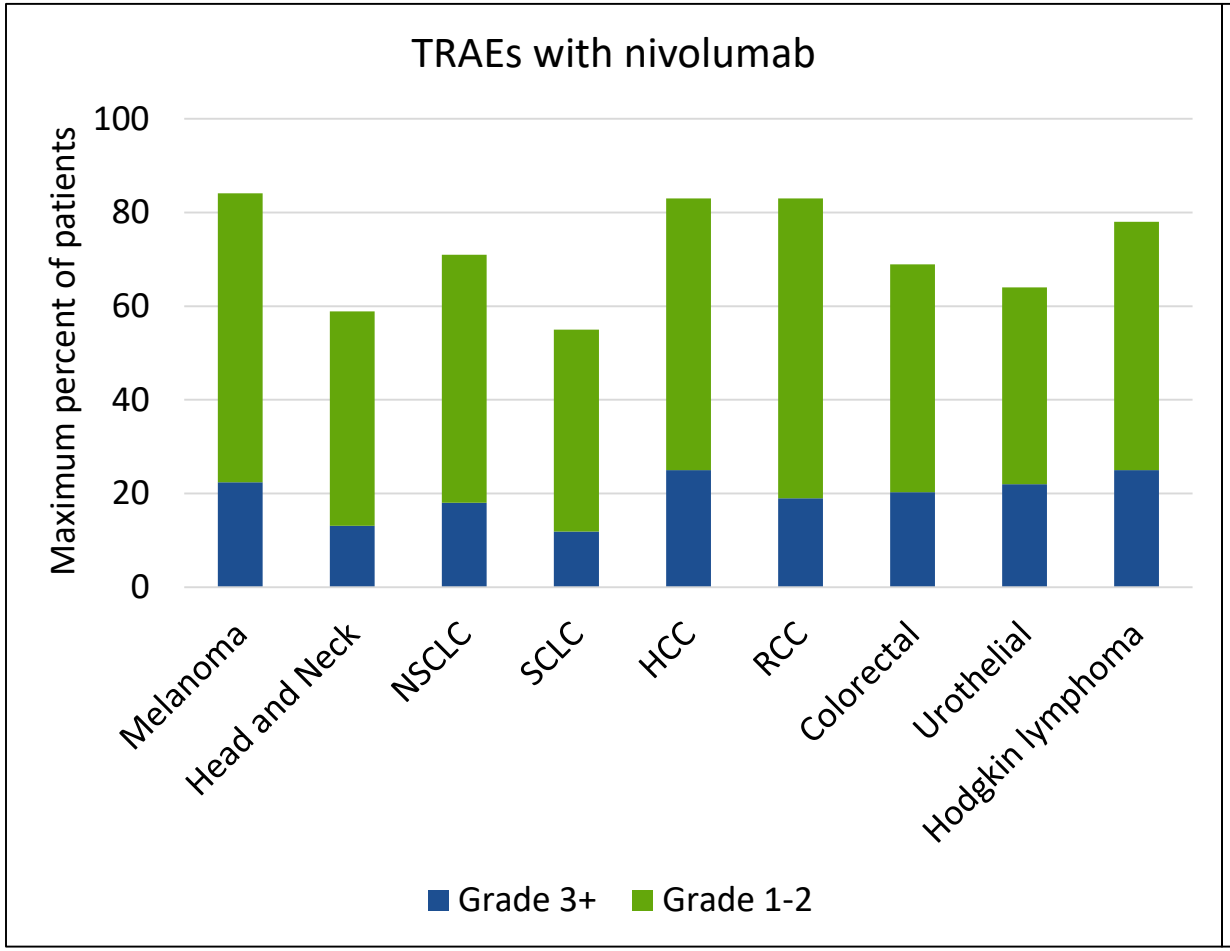
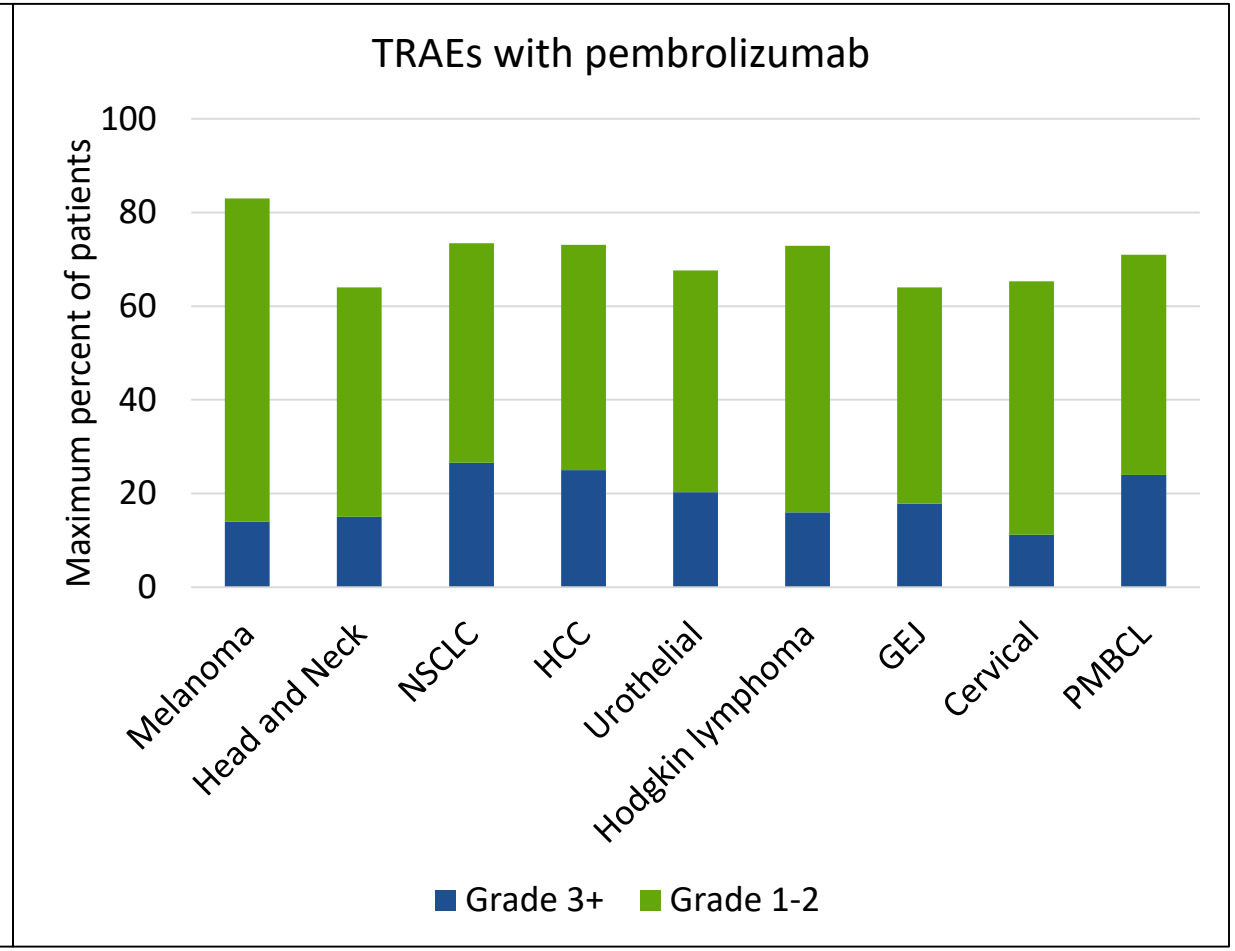
Toxicity with Immune Checkpoint Inhibitors



Arnaud-Coffin, Int J Cancer 2019

Toxicity with Immune Checkpoint Inhibitors





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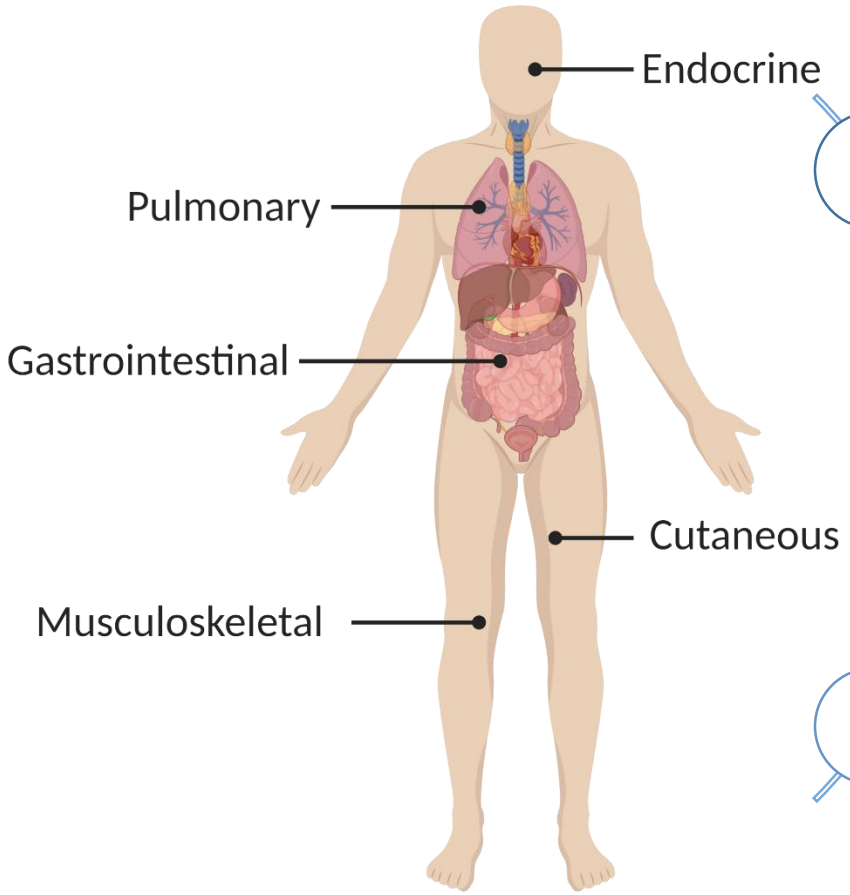
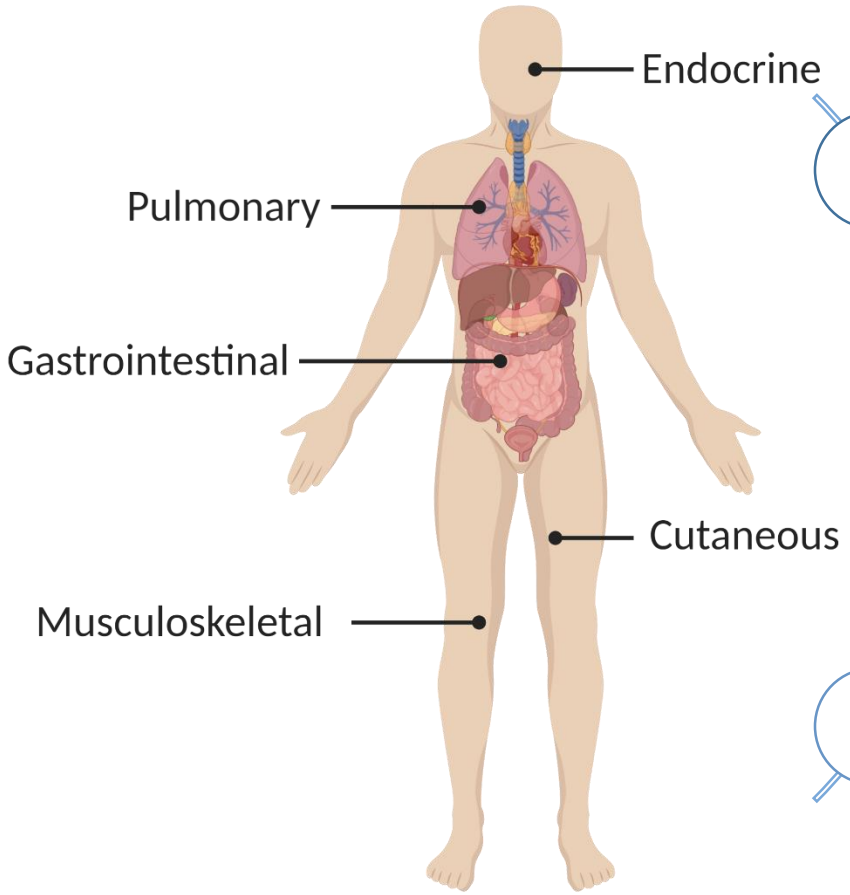
Common irAEs with ICIs



- Cutaneous: dermatitis (maculopapular, lichenoid), pruritis
- Gastrointestinal: diarrhea, colitis, hepatitis, gastritis
- Musculoskeletal: inflammatory arthritis, myositis, sicca syndrome
- Pulmonary: pneumonitis, sarcoidosis
- Endocrine: thyroid dysfunction, hypophysitis, Type 1 diabetes

Puzanov and Diab, JITC 2017.
NCCN Guidelines. Management of Immunotherapy-Related Toxicities. Version 2.2019.

Common irAEs with ICIs



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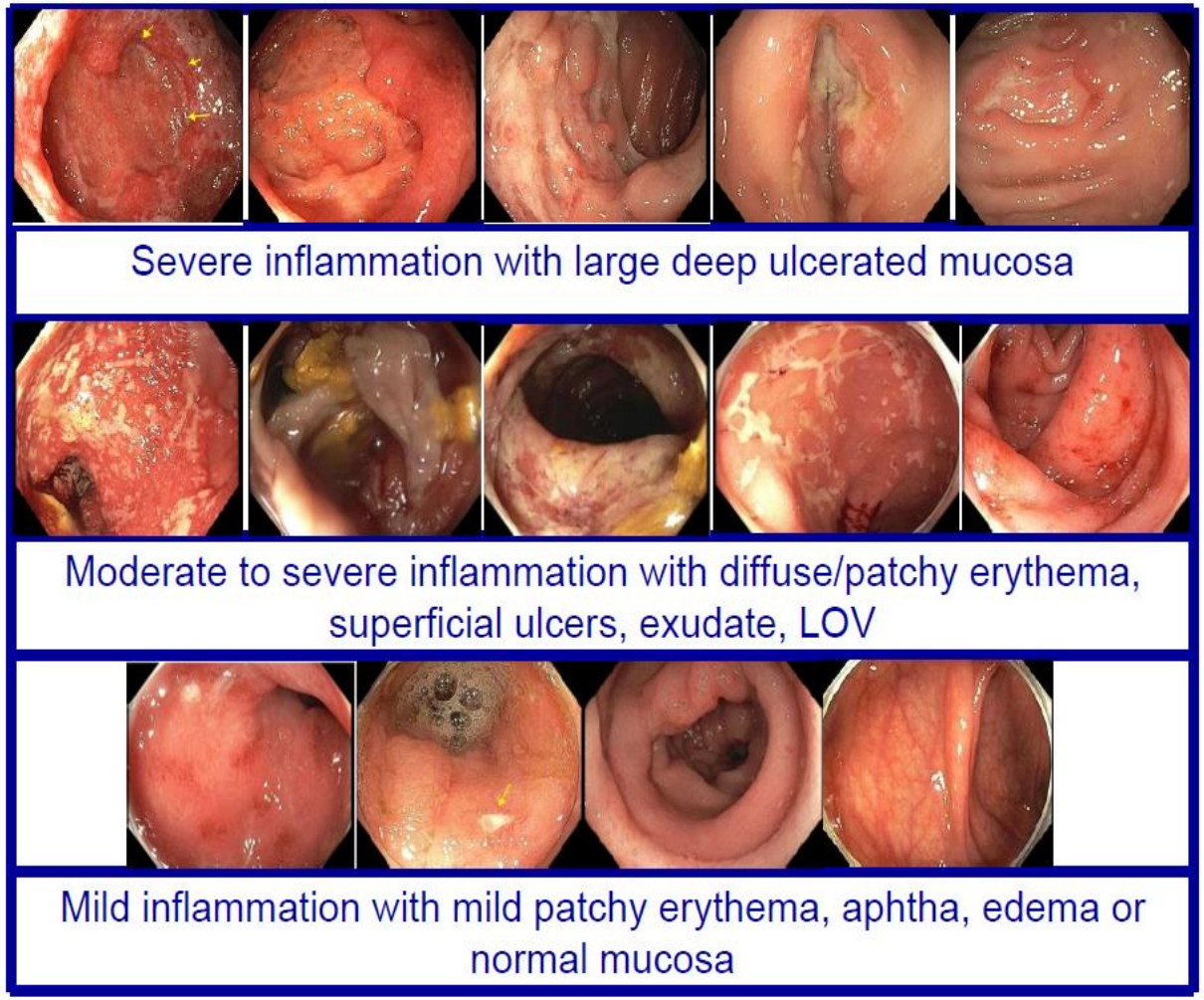
Puzanov and Diab, JITC 2017.
NCCN Guidelines. Management of Immunotherapy-Related Toxicities. Version 2.2019.

Diarrhea/Colitis

- Diagnostic evaluation
  - Rule out alternative diagnosis: C.difficile, other GI infections
  - Diarrhea while on ICIs should prompt suspicion of immune-mediated colitis
  - Consider testing with colonoscopy

- Management
  - Low threshold for starting corticosteroids given risk for bowel perforation; typical dose is prednisone 1-2 mg/kg/day (or equivalent)
  - No benefit for corticosteroid pre-treatment (budesonide)
  - Colitis that is slow to improve/refractory to steroids: treat with anti-TNF
  - Infliximab 5mg/kg q14 days (1-3 doses typically required)



Wang et al, *JITC* 2018

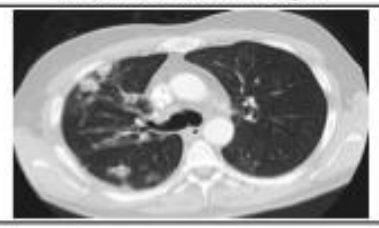
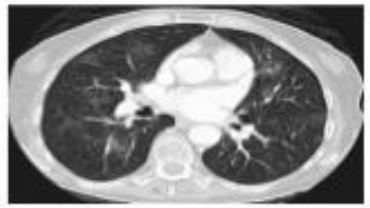
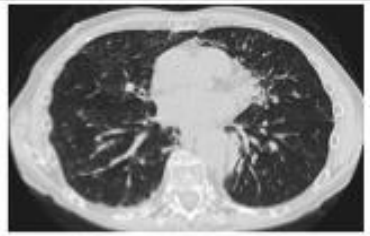
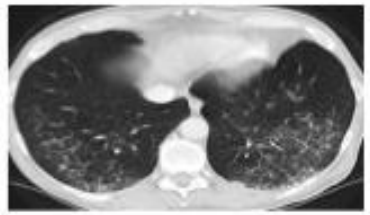
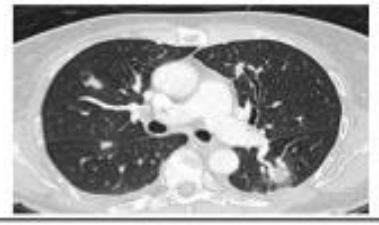
Hepatitis

- Hepatitis is often asymptomatic, but can lead to treatment discontinuation
- Elevations in AST and/or ALT
- Typically 6-14 weeks after treatment

Grade 1	Grade 2	Grade 3	Grade 4
• Liver function tests weekly	• Liver function tests weekly • Corticosteroids 0.5 mg/kg/day	• Liver function tests every 1-2 days • Withhold ICIs • Corticosteroids 1-2 mg/kg/day	• Liver function tests every 1-2 days • Discontinue ICIs • Corticosteroids 1-2 mg/kg/day
	• Diagnostic testing includes iron studies, autoimmune hepatitis panel and viral hepatitis panel • Taper steroids over 4-6 weeks once LFTs revert to grade $\leq$ 1 • If LFTs do not improve or recur after taper, may administer azathioprine or mycophenolate mofetil • Infliximab should not be used, given risk for hepatotoxicity		

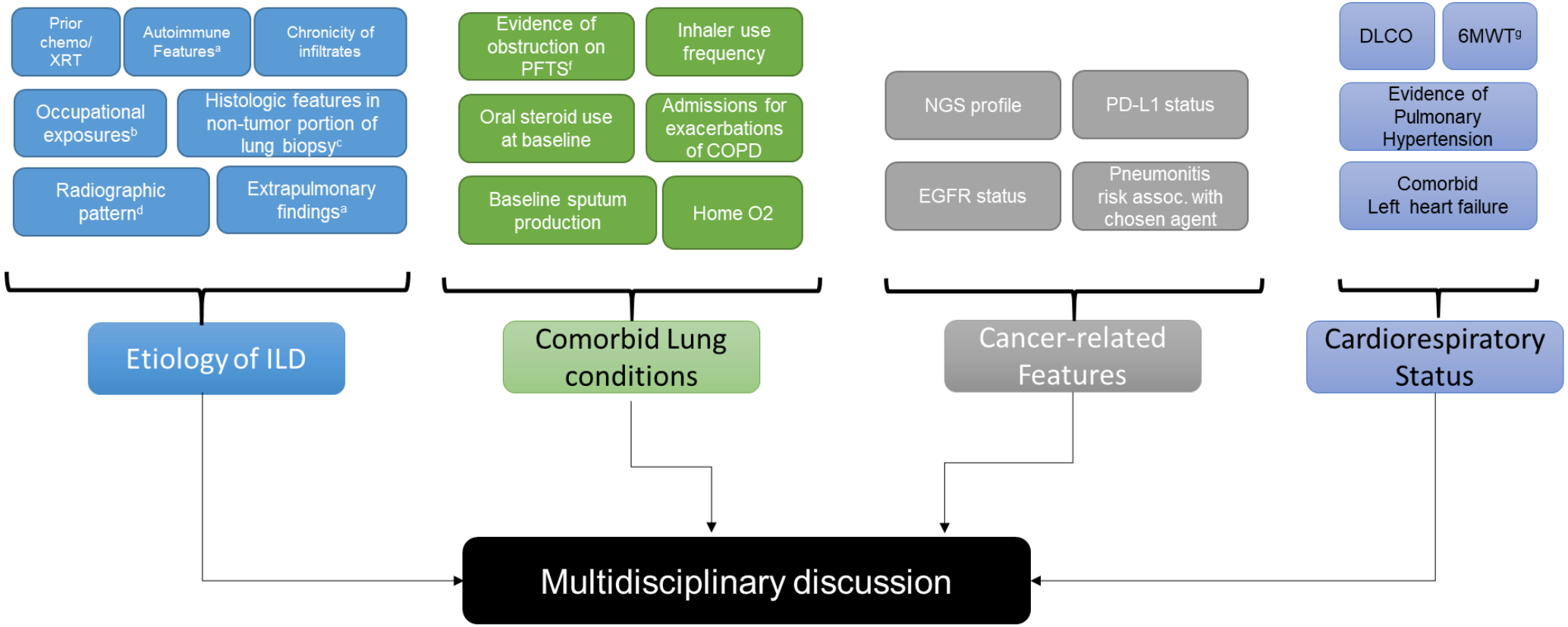
Pneumonitis

- Diagnostic evaluation
  - Symptoms: persistent dry cough, dyspnea on exertion
  - Rule out alternative diagnosis: infection, malignancy
  - Computed tomography
- Management
  - Can escalate quickly, so prompt symptom reporting is important
  - Withhold drug for low-grade
  - Corticosteroids with close follow-up
  - Additional immunosuppression may be needed

Radiologic Subtypes	Representative Image
Cryptogenic-Organizing Pneumonia-like (COP-like) (n=5, 19%)	
Ground Glass Opacifications (GGO) (n=10, 37%)	
Interstitial Type (n=6, 22%)	
Hypersensitivity Type (n=2, 7%)	
Pneumonitis Not-Otherwise Specified (n=4, 15%)	

Naidoo et al, *J Clin Oncol* 2016
Suresh, Naidoo et al, *J Thoracic Oncol* 2018

Discerning Pneumonitis from Other Diagnoses

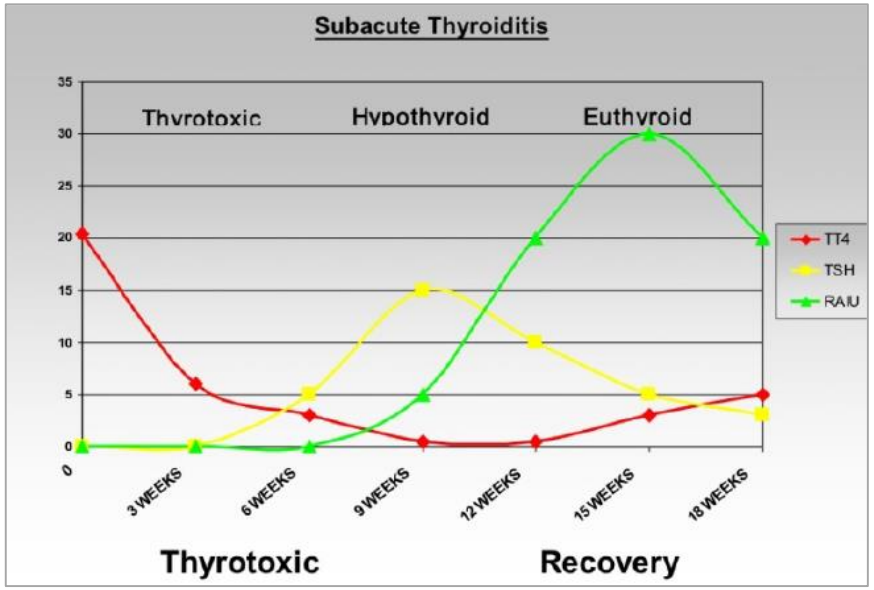


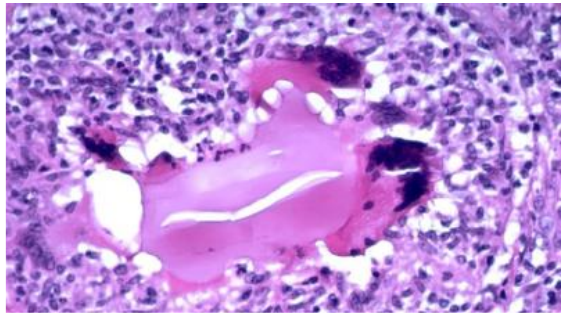
[a] Rashes (Gottron's papules, Heliotrope rash), evidence of synovitis, family history of RA/SLE, history of dry eyes/mouth, Raynaud's phenomenon
[b] Steelworkers, farmers, exposures to heavy metals, organic fumes, dusts, birds, etc. [c] such as poorly-formed granulomas, lymphocytic aggregates
[d] NSIP vs UIP-pattern, evidence of air-trapping, lobar dominance. [f] may present as complex obstruction (TLCpp – FVCpp > 15).

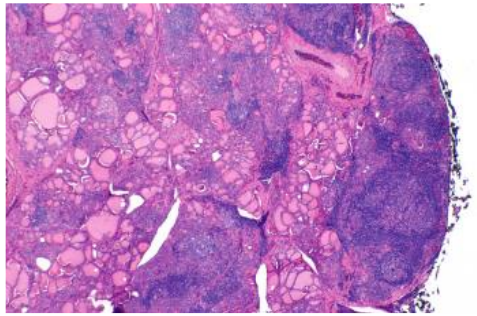
Naidoo, Suresh, The Oncologist 2020.

Thyroid Dysfunction

- Hyperthyroid Phase
  - Leaky thyroid, variable symptoms
  - 2-6 weeks duration
- Hypothyroidism Phase
  - Recovery of depleted gland
  - Symptoms: fatigue, hair and skin changes, fluid retention, constipation
  - Transient or permanent
- Management
  - Hormone replacement
  - Endocrinology consultation
  - ICI does not need to be held if this is the only irAE



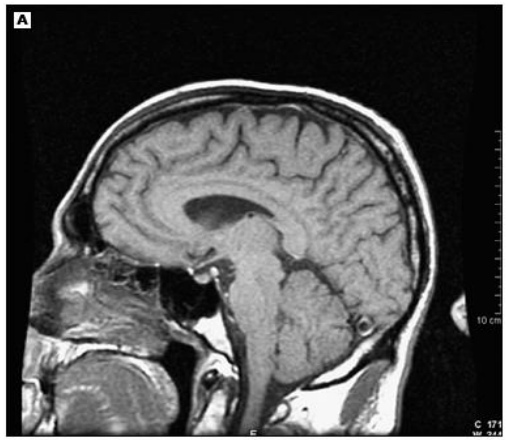




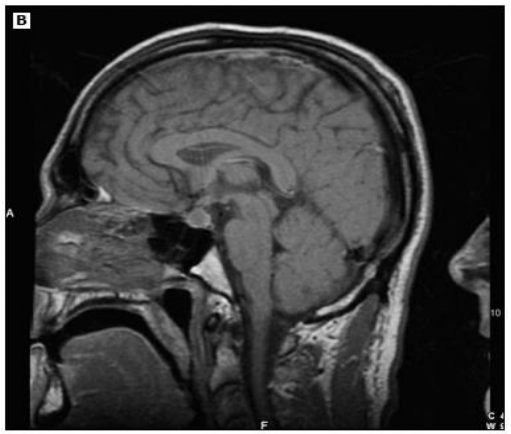
Kobayashi et al, *J Endoc Soc* 2018

Hypophysitis

- Diagnostic workup
  - Symptoms:
    - Due to increased intracranial pressure: headache, nausea, blurry vision
    - Due to hormonal deficit: fatigue, weakness, hypotension
  - Lab tests: ACTH, TSH, FSH, LH, GH, prolactin
  - Differentiate from primary adrenal insufficiency and hypothyroidism by lab results
  - Enhancement/swelling of pituitary on imaging
- Management
  - Hormone supplementation



06/30/04 - Baseline (4.5 mm)



12/03/04 - Headache/fatigue (10.8 mm)

Ryder et al, Endocr Relat Cancer 2014

Pre-Treatment Screening Recommended by SITC

- Patient History
  - Autoimmune, infectious, endocrine, organ-specific diseases
  - Baseline bowel habits
- Dermatologic
  - Full skin and mucosal exam
- Pulmonary
  - Baseline O_2 saturation
- Cardiovascular
  - ECG
  - Troponin I or T
- Blood tests
  - CBC with diff
  - CMP
  - TSH and free T4
  - HbA1c
  - Total CK
  - Fasting lipid profile
  - Infectious disease screen:
    - Hepatitis serologies
    - CMV antibody
    - HIV antibody and antigen (p24)
    - TB testing (T-spot, quantiferon gold)

Puzanov & Diab, JITC 2017.

Potential Additional Screening for High-Risk Patients

- Endocrine tests
  - 8 am cortisol and ACTH
- Cardiac tests
  - Brain natriuretic peptide (BNP) or N-terminal pro B-type natriuretic peptide (NT pro-BNP)
- Pulmonary tests
  - PFTs
  - 6MWT

Puzanov & Diab, JITC 2017.

Approach to Treatment

- Treatment approach is guided by grading of specific toxicity
- Resources for grading:
  - SITC Toxicity Management Working Group
  - Common Terminology Criteria for Adverse Events
  - National Comprehensive Cancer Network
- 1st line for **MOST** irAEs is systemic high-dose corticosteroids
  - Endocrine toxicities managed with hormone replacement
  - Some grade 1-2 irAEs may respond to topical steroids (dermatologic, ophthalmologic)
- OTC drugs may not be appropriate for managing symptoms
  - i.e. loperamide for colitis may result in bowel perforation and mask underlying symptoms

General Corticosteroid Management

Grade of irAE	Corticosteroid Management	Additional Notes
1	Usually not indicated	Continue immunotherapy
2	• Start **prednisone 0.5-1 mg/kg/day** (or equivalent dose of IV methylprednisolone) • If no improvement in 2-3 days, **increase dose** to 2 mg/kg/day • Once improved to ≤grade 1, start **4-6 week steroid taper**	• **Hold immunotherapy** during corticosteroid use • **Continue immunotherapy** once resolved to ≤grade 1 and off corticosteroids • Start proton pump inhibitor for GI prophylaxis

Puzanov & Diab, JITC 2017.

General Corticosteroid Management

Grade of irAE	Corticosteroid Management	Additional Notes
3	• Start **prednisone 1-2 mg/kg/day** (or equivalent dose of IV methylprednisolone) • If no improvement in 2–3 days, **ADD additional** immunosuppressant • Once improved to ≤ grade 1, start **4–6-week steroid taper**	• **Hold immunotherapy**; if unable to taper steroids over 4-6 weeks, **discontinue immunotherapy** • Start proton pump inhibitor for GI prophylaxis • Add PJP prophylaxis if more than 3 weeks of immunosuppression expected (>30 mg prednisone or equivalent/day)
4		• **Discontinue immunotherapy** • Start proton pump inhibitor for GI prophylaxis • Add PJP prophylaxis if >/= 4 weeks of immunosuppression expected (>/=20 mg prednisone or equivalent/day)

Puzanov & Diab, JITC 2017.

Additional Immunosuppressives for Specific Toxicities

Colitis

Infliximab
anti-TNF-α antibody
Dose: 5 mg/kg; 2nd dose may be administered after 2 weeks

Vedolizumab
A4β7 inhibition; gut-selective
Dose: 300 mg; repeat dose at 2 and 6 weeks

Pneumonitis

Mycophenolate mofetil
Inhibits T and B cell proliferation
Dose: 1 g twice per day

High dose intravenous immunoglobulin (hdIVIG)

Cutaneous

Topical tacrolimus
Calcineurin inhibitor

Indication-specific treatments
Pemphigus or bullous pemphigoid: rituximab
Eczema: dupilumab
Lichenoid rash: infliximab
Urticaria: omalizumab

Abu-Sbeih H. JITC. 2018.
NCCN Guidelines. Management of immunotherapy-related toxicities. Version 2.2019.

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Uncommon irAEs with ICIs

Cardiovascular:

Myocarditis, pericarditis, arrhythmias

Renal:

Interstitial nephritis, granulomatous nephritis

Endocrine:

Adrenal insufficiency, pancreatic insufficiency, type 1 diabetes mellitus

Hematologic:

Hemolytic anemia, red cell aplasia, neutropenia, thrombocytopenia

Neurologic:

Myasthenia gravis, Guillain-Barré syndrome, peripheral neuropathies

Ophthalmologic:

Uveitis, episcleritis, conjunctivitis

Puzanov and Diab, JITC 2017.
NCCN Guidelines. Management of immunotherapy-related toxicities. Version 2.2019.

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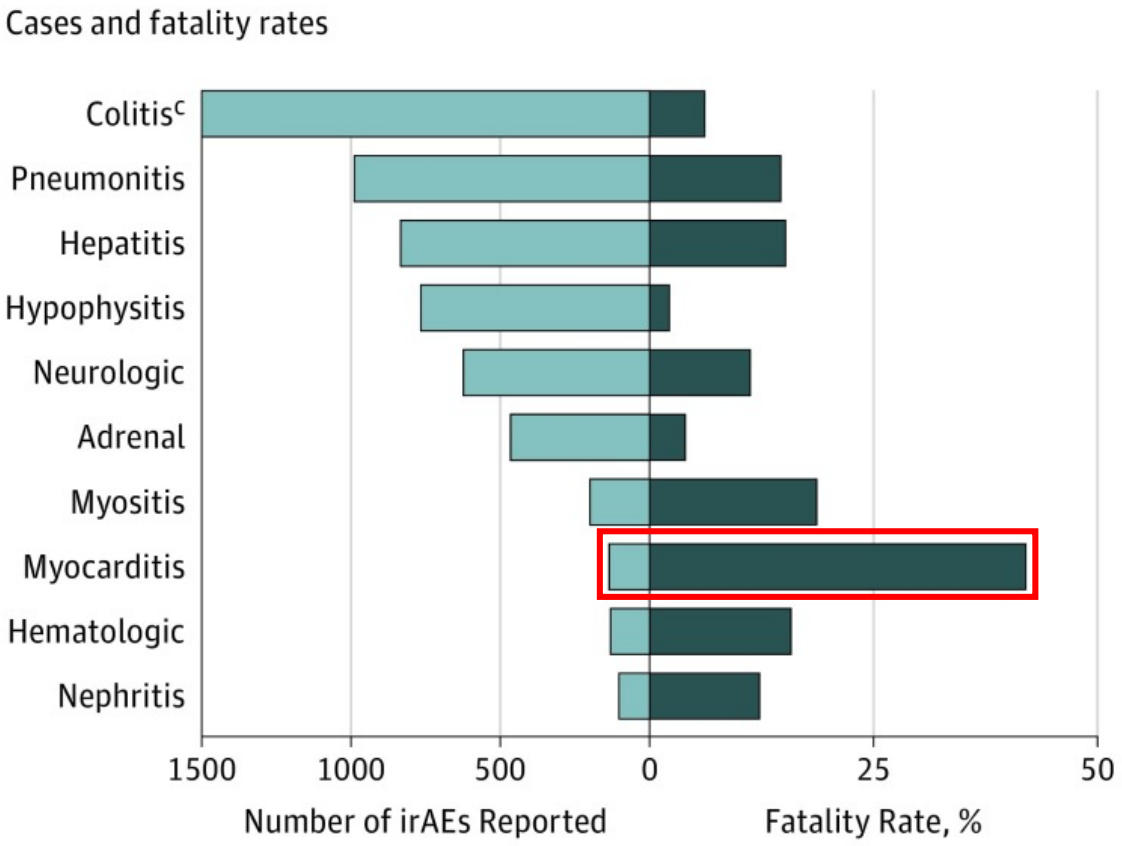
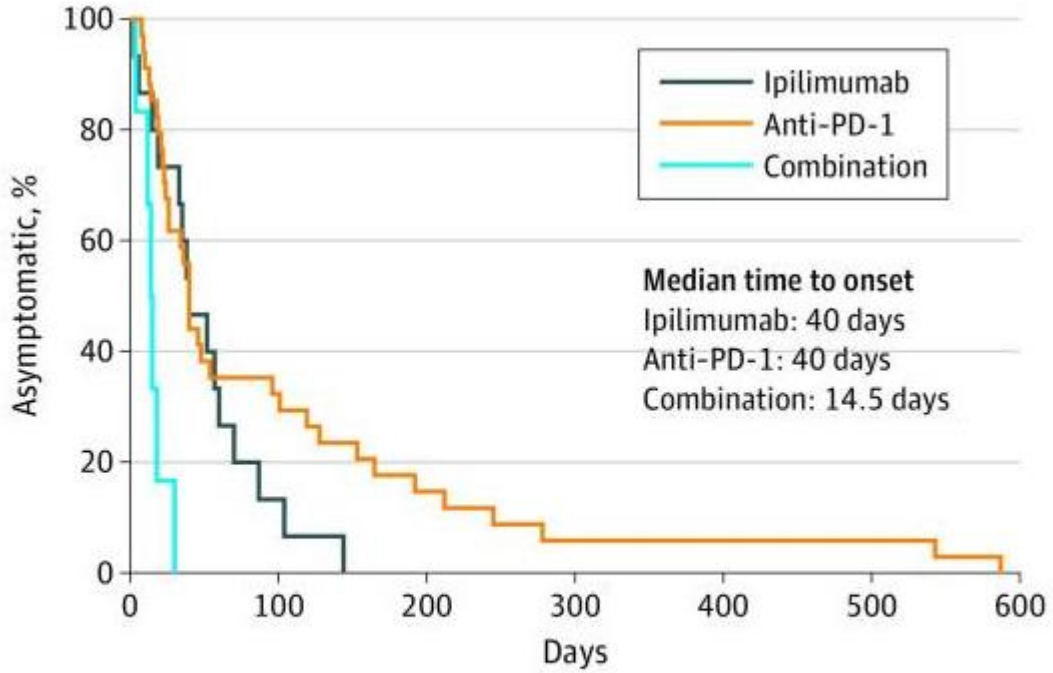
Fatal Events with ICIs



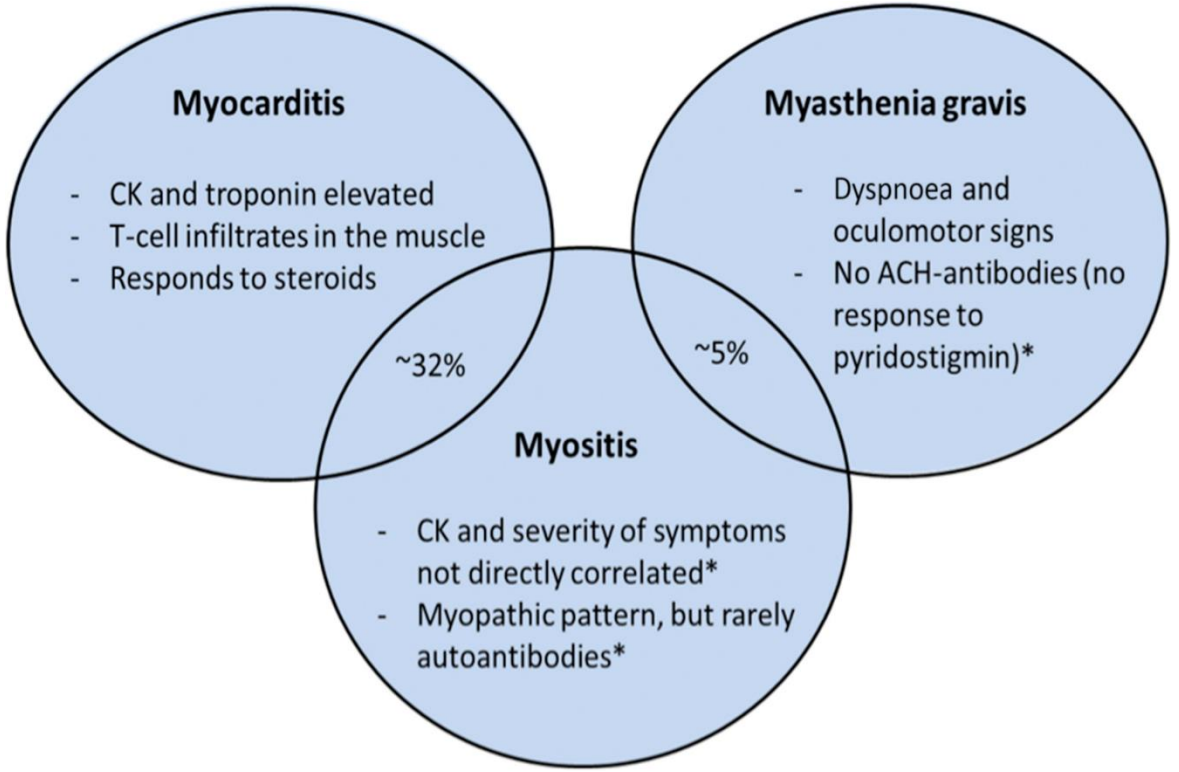


No. at risk							
Ipilimumab	15	2	0	0	0	0	0
Anti-PD-1	34	11	5	2	2	2	0
Combination	6	0	0	0	0	0	0

Wang et al, JAMA Oncol 2018.

Myocarditis

- More common with anti-CTLA-4 than anti-PD-1, but highest with combination
- Symptoms: dyspnea, chest pain, fatigue, myalgia, palpitations, syncope, dizziness
- Imaging findings usually normal
- Increased serum troponin in almost all patients – high suspicion of ICI-associated myocarditis!
- Management includes:
  - Withholding immunotherapy
  - Immunosuppressives based on grade of myocarditis
  - Heart failure support
- Often overlaps with other irAEs



Moreira et al, *Eur J Cancer* 2018
Naidoo et al, *JNCCN 2019*

Type 1 Diabetes

- Diagnostic workup
  - Most common with PD-1 pathway inhibitors
  - Symptoms: severe and sudden onset of hyperglycemia, diabetic ketoacidosis
  - Monitor glucose levels at each dose of immunotherapy
- Management
  - Typically do not respond to immunosuppressives
  - Requires insulin therapy

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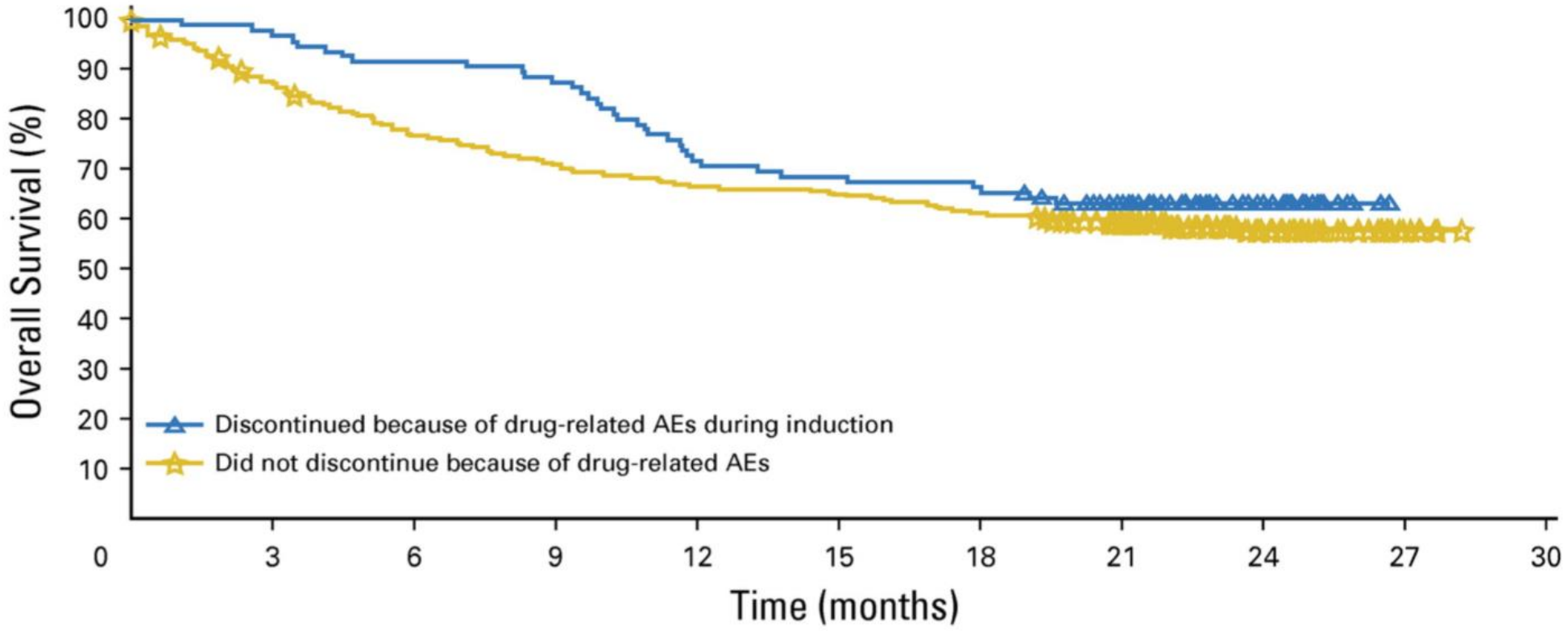
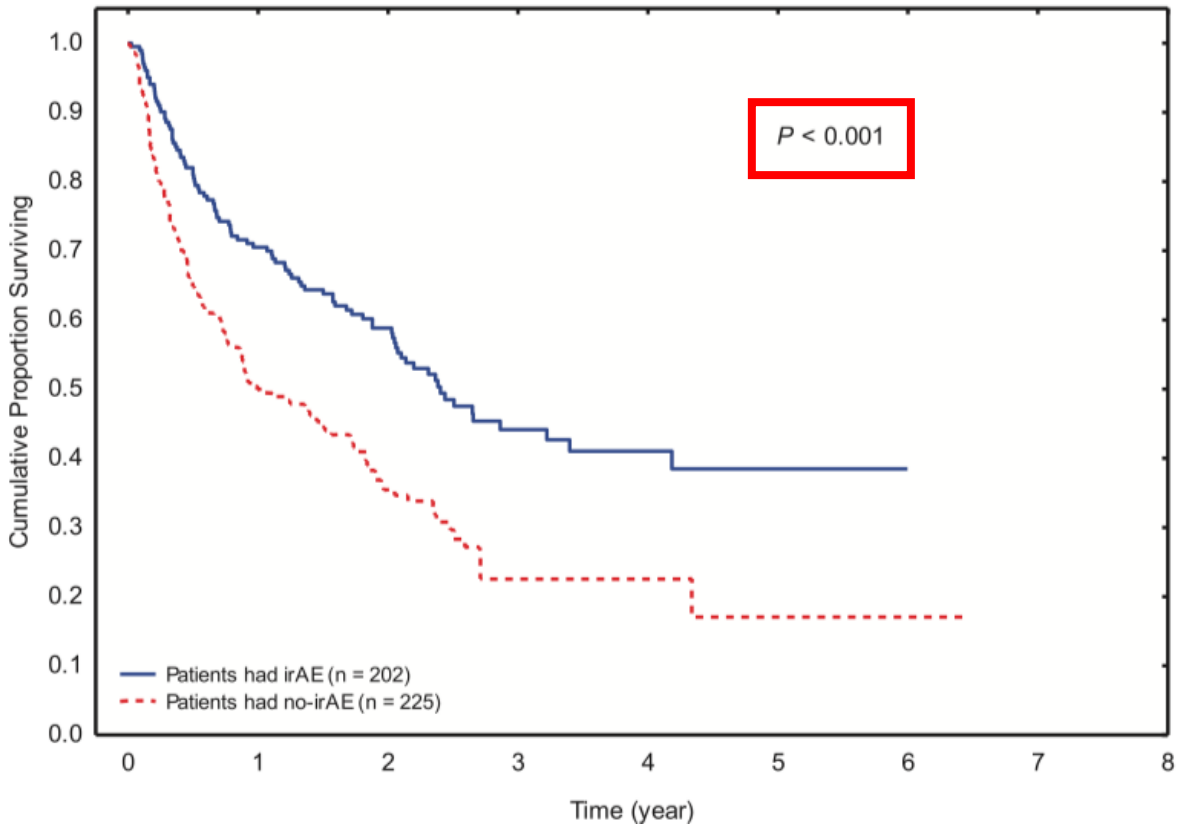
Effect of irAEs on Patient Outcomes

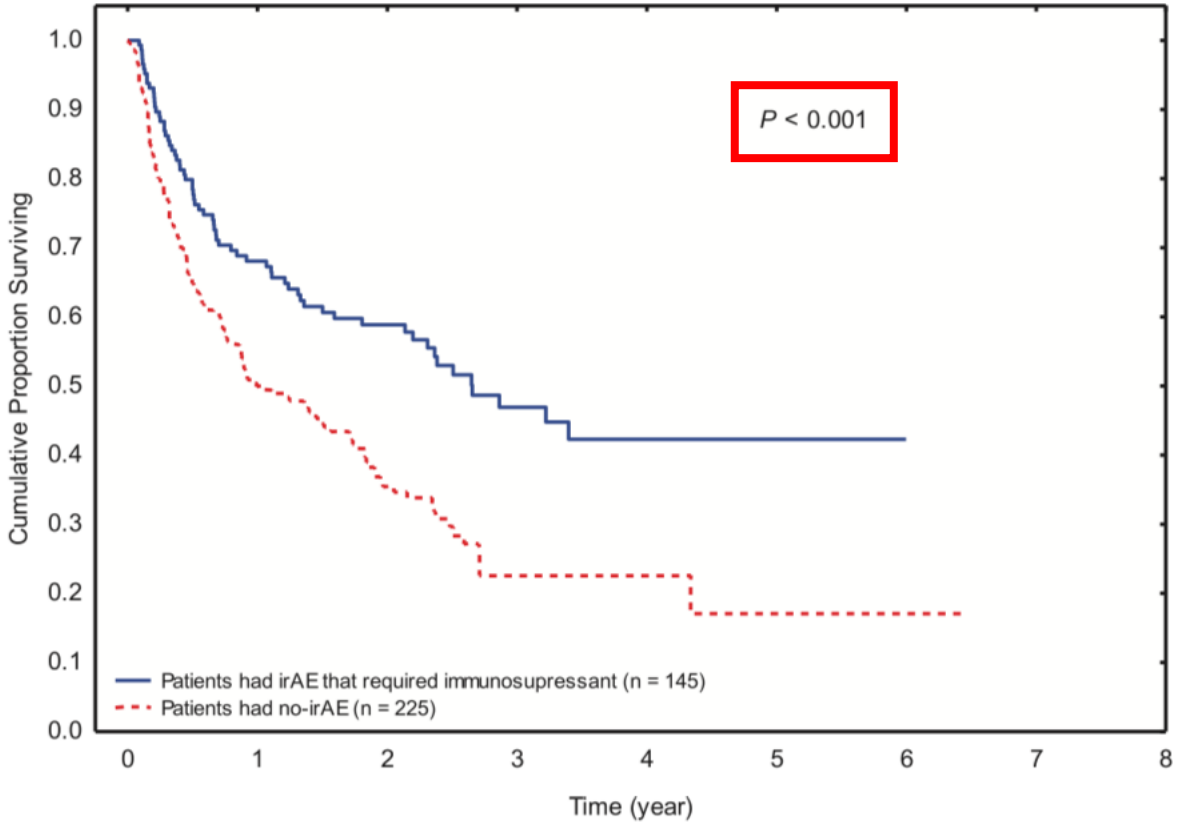


No significant difference in survival in melanoma patients who discontinued ipilimumab + nivolumab due to irAEs versus those who did not discontinue treatment

Schadendorf D. J Clin Oncol 2017

Autoimmunity as a Prognostic Marker?





Based on **retrospective** data, patients who experience irAEs (regardless of needing treatment) may have better outcomes compared to patients who do not experience irAEs

Abu-Sbeih, J Immunoth Prec Oncol 2018.

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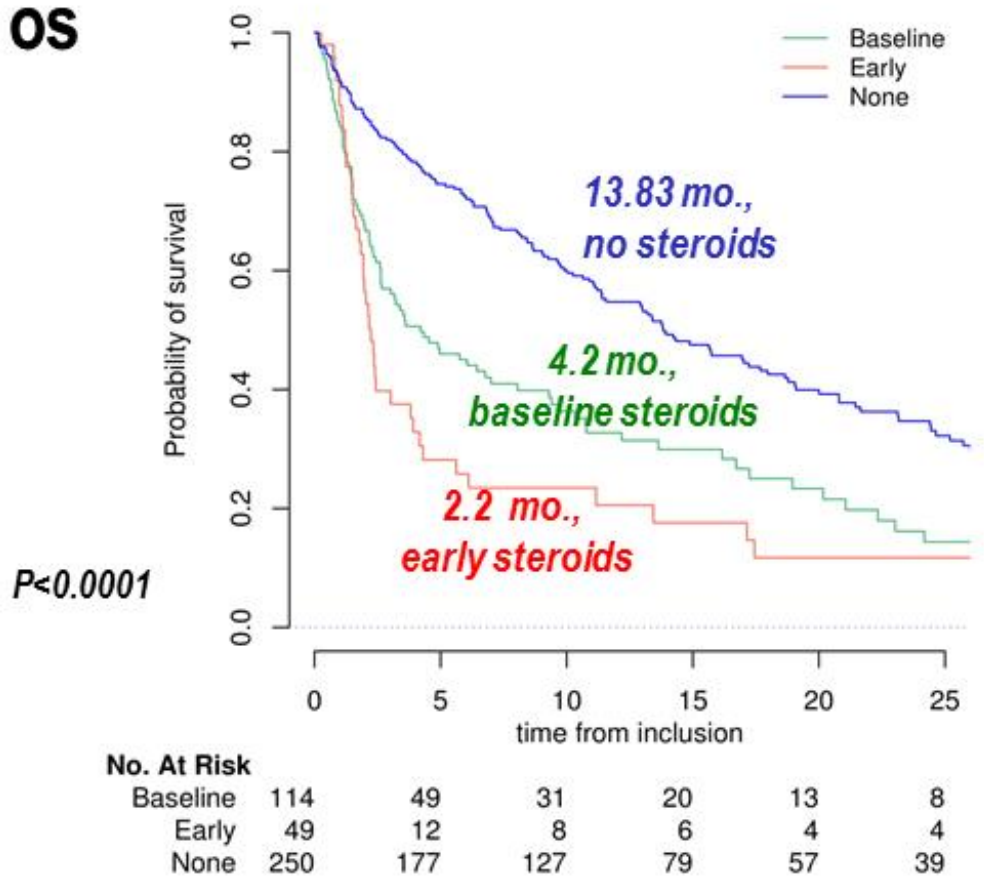
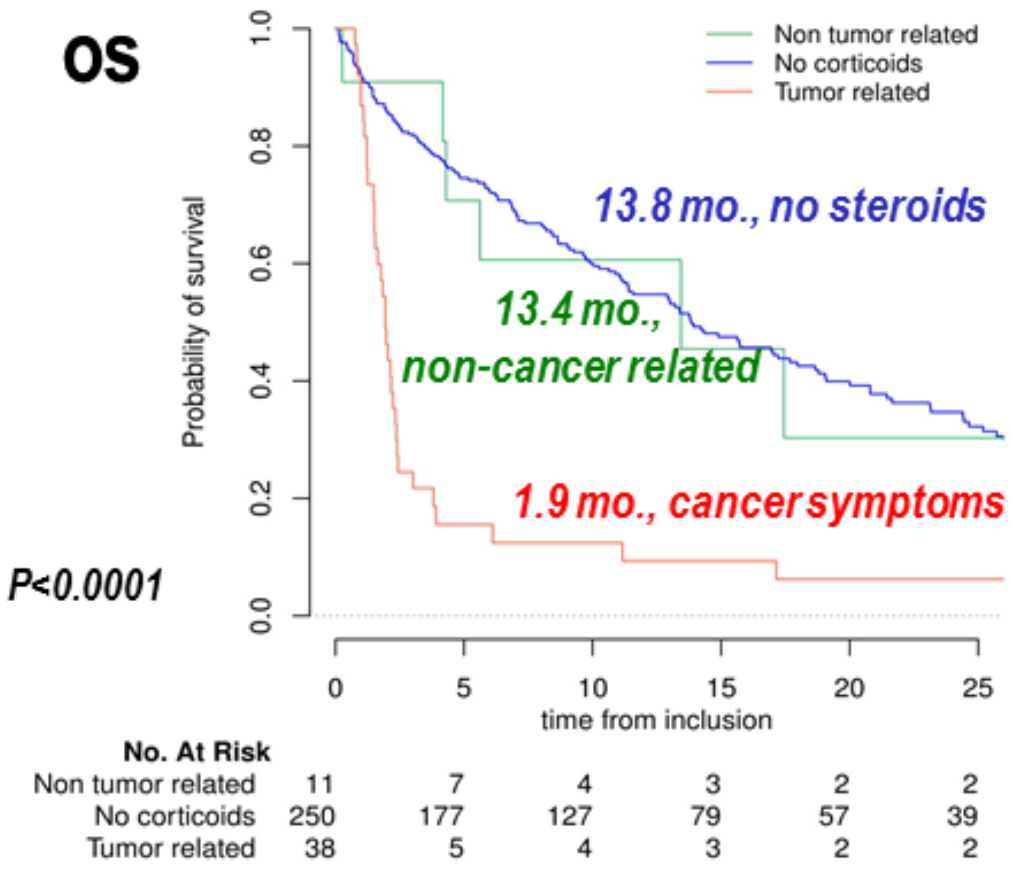
Impact of Steroid Management on Patient Outcomes





De Giglio, Mezquita et al, ESMO-IO 2020.

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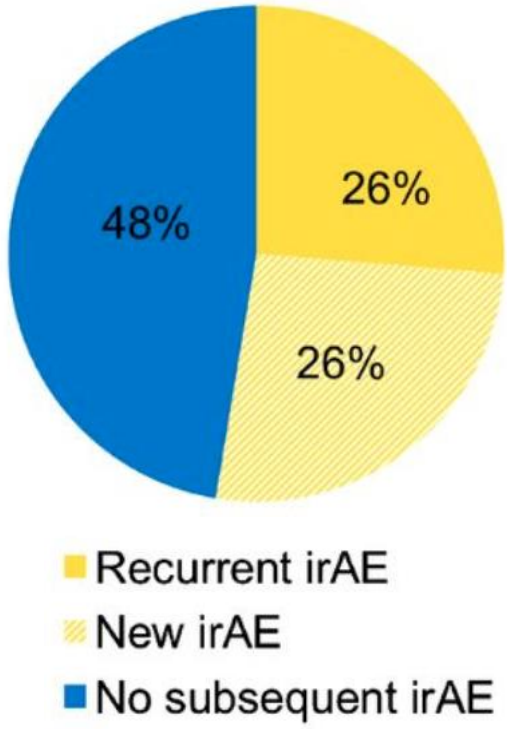
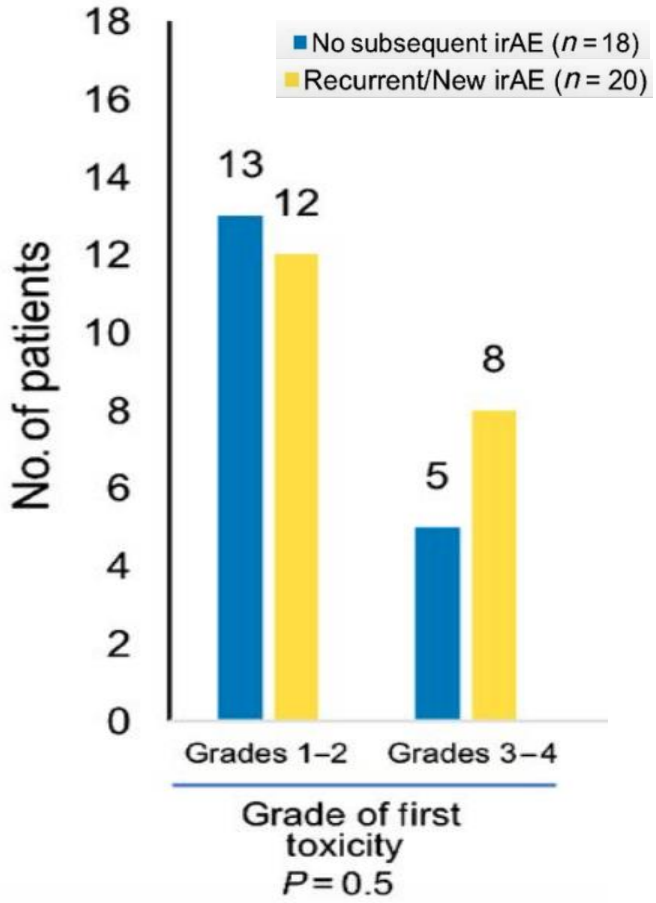
Rechallenging with ICIs After irAEs

- Patients should not be rechallenged until irAE resolved to grade ≤1
- Re-challenge with anti-PD-1/L1 after anti-CTLA-4 ± anti-PD-1 likely safe
- Caution in re-challenging with same ICI in patients who previously had grade 3-4 irAEs





Santini FC. Cancer Immunol Res 2018.

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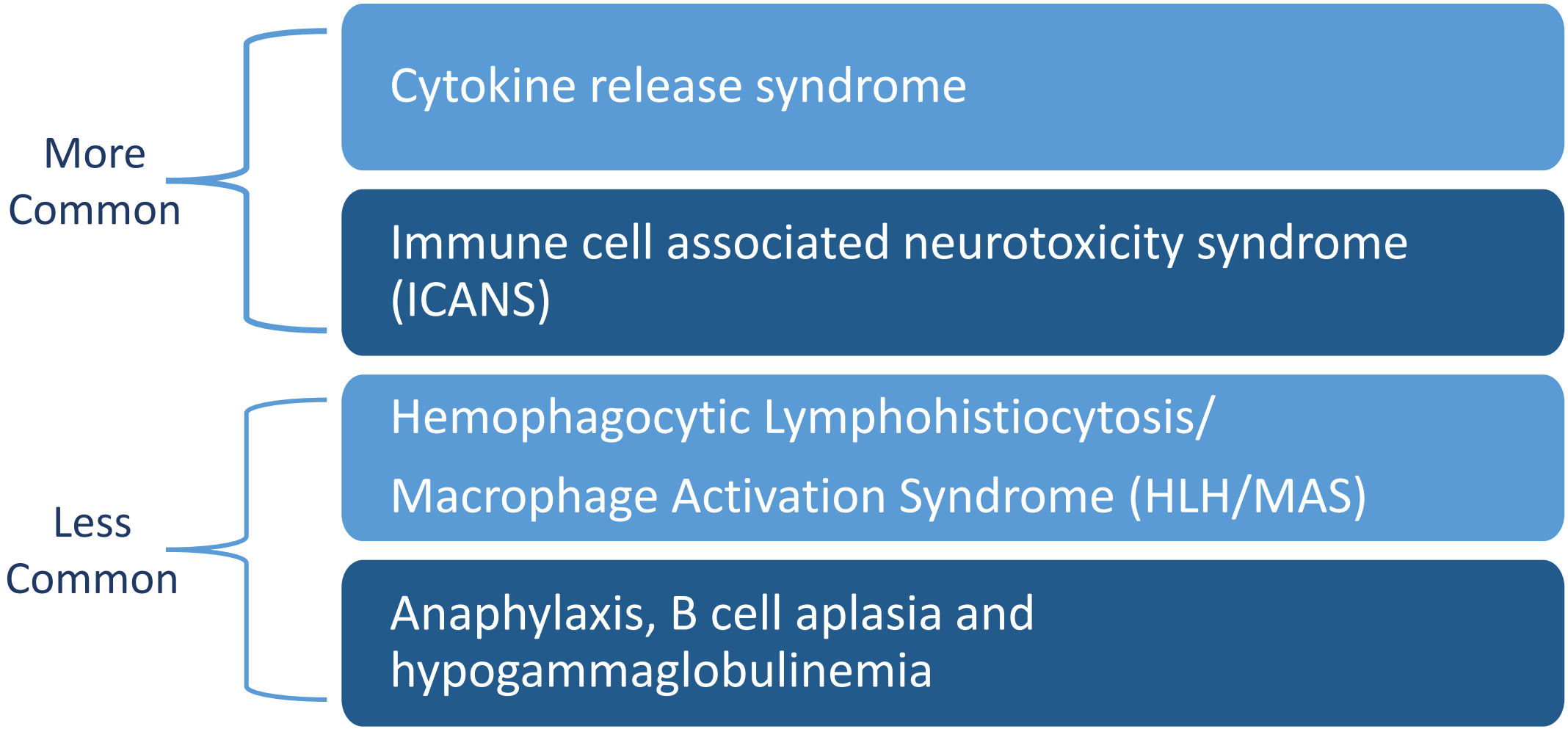
- Case studies

CAR T-Cell Related Toxicities



NCCN Guidelines. Management of immunotherapy-related toxicities. Version 2.2019.

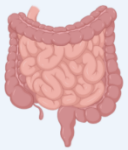
CRS and Neurotoxicity

- Should not be viewed as two unrelated adverse events
  - Overlapping toxicities from excessive immune activation
  - May occur together or exclusive of one another
  - However, they do have distinct timing and responses to treatment
- Risk factors for both include:
  - High disease burden
  - Higher infused CAR-T cell dose
  - High intensity lymphodepletion regimen
  - Pre-existing endothelial activation
  - Severe thrombocytopenia

Santomasso BD. Cancer Discov 2018.
Wang Z. Biomark Res. 2018.

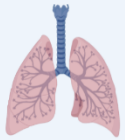
Cytokine Release Syndrome

Gastrointestinal
- Nausea/vomiting
- Diarrhea
- Anorexia



Skin
- Rash

Respiratory
- Tachypnea
- Hypoxia
- Pulmonary edema

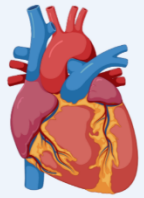


Constitutional
- Fever +/- rigors
- Malaise/fatigue
- Myalgias
- Arthralgias
- Headache

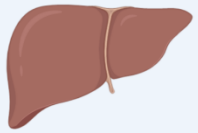
Cytokine Release Syndrome symptoms

Coagulation
- Elevated D-dimer
- Hypofibrinogenemia +/- bleeding

Cardiovascular
- Tachycardia
- Hypotension
- Capillary leak
- Widened pulse presssure
- Increased cardiac output (early)
- Potentially diminished cardiac output (late)



Hepatic dysfunction
- Transaminitis
- Hyperbilirubinemia



Renal function
- Azotemia

Riegler LL. Ther Clin Risk Manag 2019.

Cytokine Release Syndrome

- Occurs in ~70% of patients; severe = 12-47%
  - Median onset 2-3 days after infusion, typical duration 7-8 days
- Multiple grading systems exist (MSKCC, CarTox, ASTCT)
  - Hypotension and hypoxia are main drivers of CRS severity

CRS Grade	Anti-IL-6	Steroids	Supportive Care
Grade 1 (fever > 38°C)	CRS > 3 days	N/A	• Antibiotics • GCSF if neutropenic
Grade 2 (fever/hypotension)	Tocilizumab 8mg/kg (4 doses max)	refractory hypotension Dex 10mg q6	• IV fluids, pressors • Manage as G3 is no improvement in 24hr
Grade 3 (+pressors)	Tocilizumab 8mg/kg (4 doses max)	Dex 10mg q6	• IV fluids, pressors, • Echocardiogram • ICU, oxygen
Grade 4 (+ventilatory support)	Tocilizumab 8mg/kg (4 doses max)	Dex 10mg q6 Methylpred 1g/day if refractory	• ICU care • Mechanical ventilation • Organ toxicity management

Neelapu et al, *Nat Rev Clin Oncol* 2018
Thompson et al, *JNCCN* 2019, NCCN guidelines
Lee et al, *Biol Blood Marrow Transplant 2018*

Neurotoxicity

- Also called CAR-T Related Encephalopathy Syndrome (CRES) or iIEC-associated neurologic syndrome (ICANS)
- Occurs in 20-64% of patients, ≥ grade 3 in 11-42%
  - Onset 4-5 days after infusion, typical duration 5-12 days

Neurotoxicity Domain	Grade 1	Grade 2	Grade 3	Grade 4
ICE score	7-9	3-6	0-2	0
Depressed level of consciousness	Awakens spontaneously	Awakens to voice	Awakens to tactile stimulus	Unrousable
Seizure	N/A	N/A	Any clinical seizure/on EEG	Prolonged/life-threatening seizure
Motor Findings	N/A	N/A	N/A	Hemi or paraparesis, deep focal motor weakness
Raised ICP/ cerebral edema	N/A	N/A	Focal edema on imaging	Diffuse cerebral edema on imaging, cranial N palsy, Cushing's triad, Decorticate posture

Wang Z. Biomark Res. 2018
Hunter BD. J Natl Cancer Inst. 2019

HLH/MAS

- Inflammatory syndrome caused by hyperactivation of macrophages and lymphocytes
- Rare; frequency reported to be as low as ~1%
- Should be managed with anti-IL-6 and corticosteroid therapy
- If no improvement after 48 hours, consider adding etoposide for additional immunosuppression
  - Dose: 75-100 mg/m^2
  - May be repeated after 4-7 days

Box 5 | **Diagnostic criteria for CAR-T-cell-related HLH/MAS**

A patient might have HLH/MAS if he/she had a peak serum ferritin level of >10,000 ng/ml during the cytokine-release syndrome phase of CAR-T-cell therapy (typically the first 5 days after cell infusion) and subsequently developed any two of the following:

- Grade ≥3 increase in serum bilirubin, aspartate aminotransferase, or alanine aminotransferase levels*
- Grade ≥3 oliguria or increase in serum creatinine levels*
- Grade ≥3 pulmonary oedema*
- Presence of haemophagocytosis in bone marrow or organs based on histopathological assessment of cell morphology and/or CD68 immunohistochemistry

Titov A. Cell Death Dis. 2018.
Neelapu SS. Nat Rev Clin Oncol. 2018.

Outline

- Incidence, onset and severity grading
- Immune checkpoint inhibitors
  - Common adverse events
  - Rare but serious adverse events
  - Impact of irAEs on cancer outcomes
- Cellular therapies
  - Adverse events and management
- Immunotherapy in special patient populations
- Case studies

Patients with Autoimmune Disorders

- Ipilimumab in melanoma patients
  - 29% experienced flare of pre-existing disorder; 29% experienced new irAEs
  - 56% experienced no flare OR additional irAEs
- PD-1 in melanoma patients
  - 38% experienced flare; 29% experienced new irAEs
  - Lower response rates in patients who remained on immunosuppressive treatment (15% vs 44%)
- Efficacy appears similar for patients with autoimmune disorders compared to those without

Kahler KC. Cancer Immunol Immunother. 2018.

ICI Use in Patients with Solid Organ or Stem Cell Transplants

- Patients who relapse after allogeneic SCT:
  - Ipilimumab: 32% response (10 mg/kg); 14% GVHD; 21% irAEs
  - Anti-PD-1: 77% response; 26% died due to new-onset GVHD
- Solid organ data is limited; most is in renal SOT patients
  - One retrospective study (n=39) reported graft loss in 81% and death in 46%
  - Also reported rapid time to rejection with median onset of 21 days
- PD-1 pathway appears to be more critical in allograft immune tolerance compared to CTLA-4 pathway

Davids MS. NEJM 2016
Haverkos BM. Blood 2017
Abdel-Wahab. JITC 2019

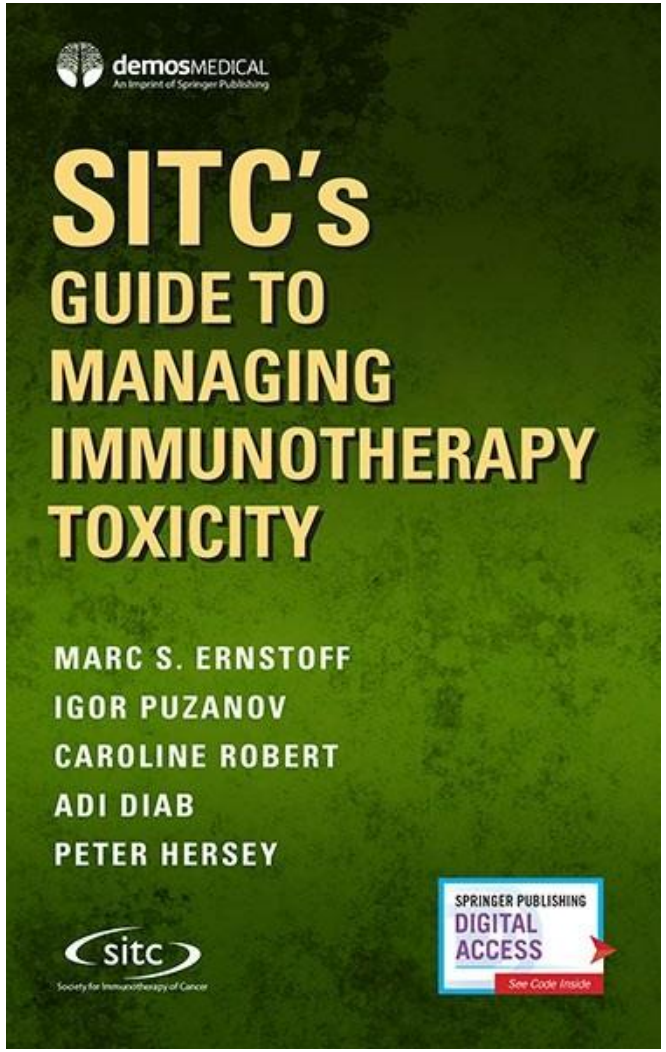
The Importance of Patient Education

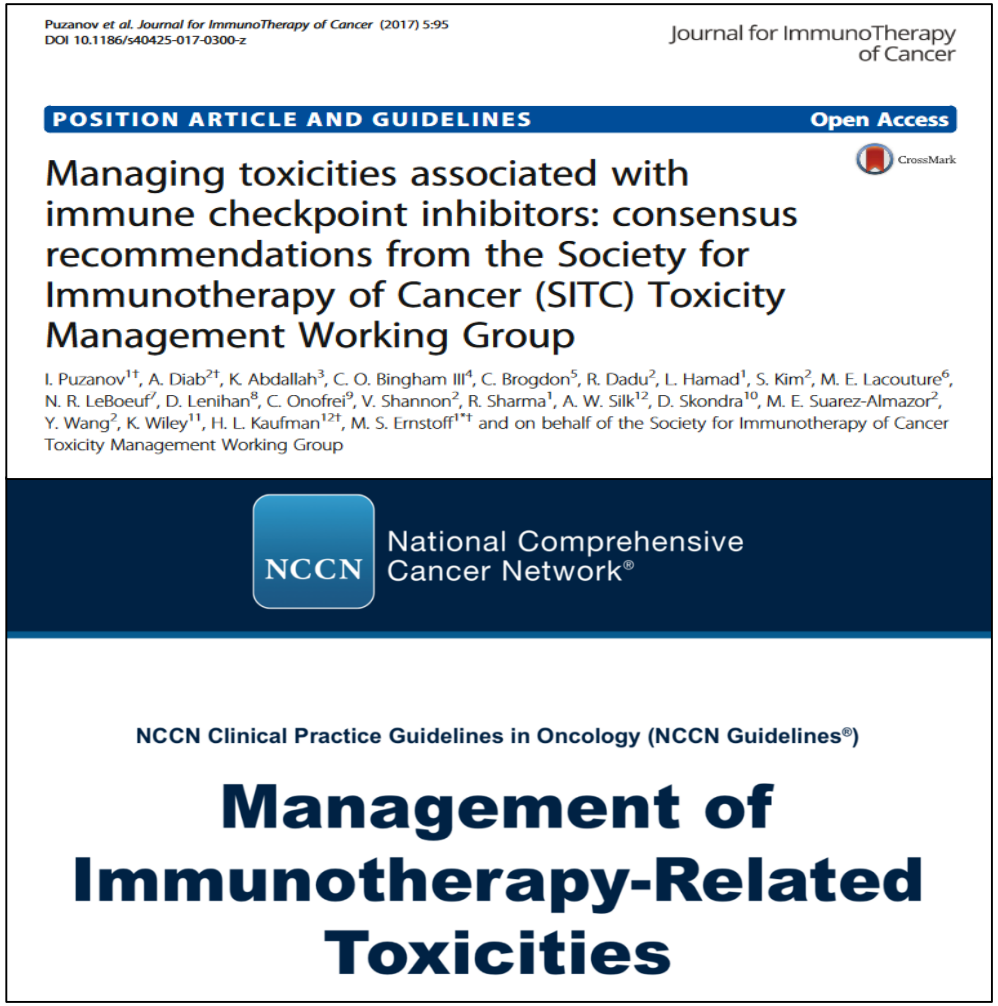
- Many immune-related adverse events can present in similar ways to other diseases, but the treatment of them is very different.
- Patients need to be able to:
  - Identify themselves as immunotherapy recipients
  - Recognize key symptoms of common/severe irAEs
  - Know when to call for assistance
- Reassure patients that irAEs will likely resolve over time (except endocrinopathies)

Education Along the Healthcare Continuum

- Patients may not go back to their original clinic for adverse event management
- Emergency departments and primary care physicians need to recognize and know how to manage irAEs
- For example, the most common irAE in emergency departments is diarrhea – recognize immune-related symptoms versus other causes (including chemotherapy related diarrhea)

Additional Resources





#LearnACI

Case Study 1

- ET is a 64 year old female with stage IV NSCLC s/p C3 nivolumab + ipilimumab. She calls in to clinic describing 5-6 watery stools daily for the past 4 days. Stool studies are drawn. C. diff and stool cultures are (-), but fecal calprotectin is 1120 (high). ET is given prednisone 1 mg/kg daily for grade 2 colitis. Her diarrhea continues to worsen over the next 3 days to 12 watery stools daily. ET is admitted to the hospital for further workup and treatment. Colonoscopy shows moderate colitis. The patient is started on infliximab and the diarrhea improves.
  - **Meds**: Methylprednisolone 80 mg IV daily, omeprazole 20 mg daily, ondansetron 8 mg q8hr PRN
- Which of the following would be the most appropriate supportive care measure to start immediately?

A. Fluconazole 200 mg daily

B. Loperamide 2-4 mg every 4 hours as needed

C. Acyclovir 400 mg twice daily

D. Sulfamethoxazole-Trimethoprim 400-80 mg daily

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Case Study 1

- ET's prednisone taper is successful. Her diarrhea resolves and daily stools return to normal frequency and consistency. She is rechallenged with nivolumab only, but calls in a week after Cycle 7 describing mild headaches and nausea with severe fatigue that makes it difficult to even walk out to her mailbox. An 8 AM endocrine panel and BG check is performed.
  - **Labs**: ACTH 3.9 (low), Cortisol 1.9 (low), TSH 0.02 (low), free T4 1.4 (normal), FSH 19.3 (low), LH 0.9 (low), BG 134 (normal)
  - **Vitals**: Wt 80 kg, Ht 167 cm, HR 94, BP 134/82, RR 15 3.9
- Which is the most appropriate initial intervention for this irAE (hypophysitis)?

A. Levothyroxine 50 mcg daily

B. Propranolol 10 mg every 4-6 hours

C. Prednisone 1 mg/kg daily

D. Hydrocortisone 20 mg in AM, 10 mg in PM

Case Study 1

- ET's prednisone taper is successful. Her diarrhea resolves and daily stools return to normal frequency and consistency. She is rechallenged with nivolumab only and feels well for several months off steroids. ET calls in a week after Cycle 9 describing mild headaches and nausea with severe fatigue that makes it difficult to even walk out to her mailbox. An 8 AM endocrine panel and BG check is performed.
  - **Labs**: ACTH 3.9 (low), Cortisol 1.9 (low), TSH 0.02 (low), free T4 1.4 (normal), FSH 19.3 (low), LH 0.9 (low), BG 134 (normal)
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Case Study 2

- MJ is a 42 year old male on pembrolizumab for BRAFm(-) metastatic melanoma. He presents after Christmas with an AST of 153 and ALT of 402; other LFTs are WNL. Per his report, he drank too much alcohol over the holiday. Thus, you decide to go forward with treatment. Three weeks later, the patient presents for the next cycle of pembrolizumab and is found to have AST 302, ALT 1406, and T. bili of 1.9. He is admitted and started on prednisone 1 mg/kg daily but after 3 days his LFTs continue to rapidly rise (AST 709, ALT 2243, T. bili 4.7). Hepatitis panel is negative. An abdominal US is clear with no evidence of blockage or hepatic metastases.
- Which of the following would be the most appropriate next step for treatment of his irAE (hepatitis)?
  - A. Mycophenolate
  - B. Infliximab
  - C. Methotrexate
  - D. IVIG

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C. Methotrexate

D. IVIG

Case Study 2

- MJ's hepatitis (secondary to pembrolizumab) resolves, and he is successfully tapered off of immunosuppression over the next 7 weeks with normal LFTs. Unfortunately, new imaging shows his cancer has progressed. Immunotherapy rechallenge is being actively considered. Due to his hospitalization, MJ is hesitant about restarting immunotherapy and would like to know the risk of another immune-related adverse event occurring upon rechallenge.
- What is the approximate risk of irAE in MJ after rechallenge with a similar anti-PD1 checkpoint inhibitor?

A. 0%
B. 25%
C. 50%
D. 75%

Case Study 2

- MJ's hepatitis (secondary to pembrolizumab) resolves, and he is successfully tapered off of immunosuppression over the next 7 weeks with normal LFTs. New surveillance imaging demonstrates an ongoing partial response to pembrolizumab. MJ's oncologist is considering immunotherapy rechallenge. However, due to his hospitalization, MJ is hesitant about restarting immunotherapy and would like to know the risk of another immune-related adverse event occurring upon rechallenge.
- What is the approximate risk of irAE in MJ after rechallenge with a similar anti-PD1 checkpoint inhibitor?

A. 0%
B. 25%
C. 50%
D. 75%

Acknowledgements

- Some figures created using Biorender.com