Society for Immunotherapy of Cancer

Advances in Cancer Immunotherapy™

Cancer Immunotherapy In Practice

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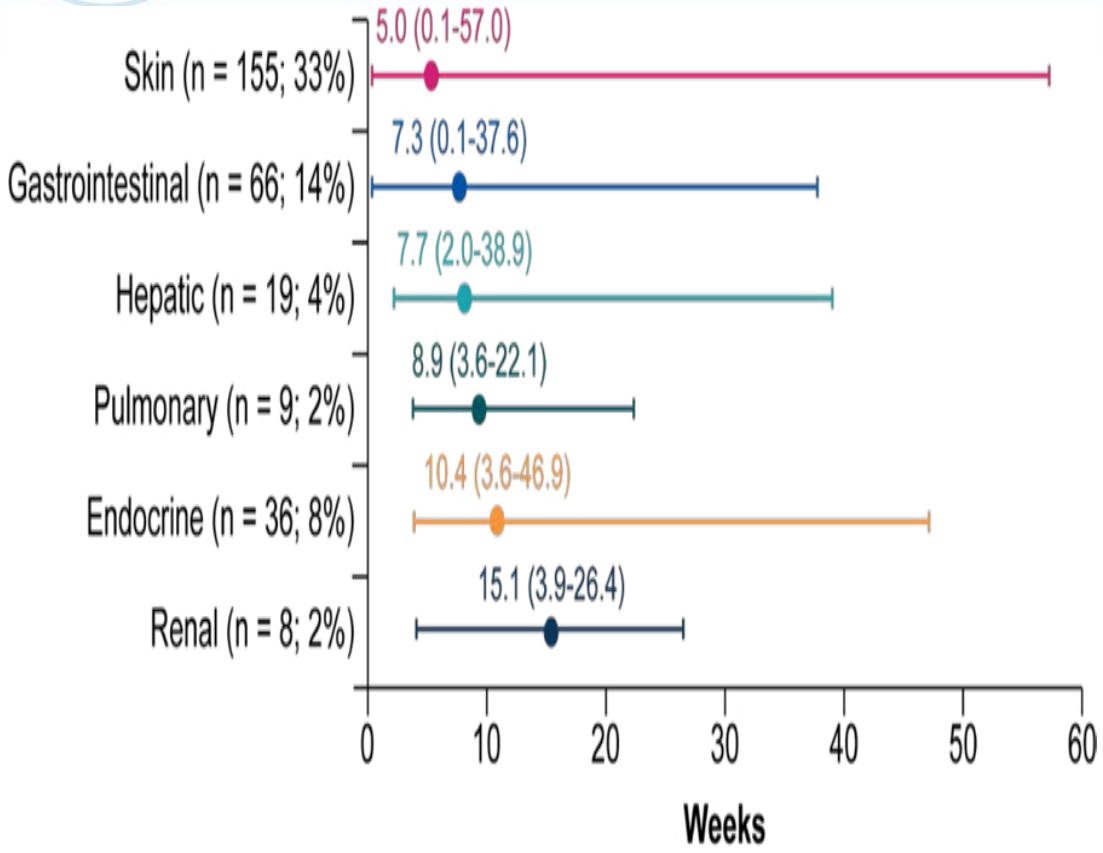
Disclosures

- Consulting Fees: AIM at Melanoma Foundation
- I will be discussing non-FDA approved indications during my presentation.

Outline

- General Considerations for irAE
- Considerations for Pre-treatment visit/Establishing a “Baseline”
- Focused and Systematic Follow-up
- Special consideration: Adrenal Insufficiency
- Important Steroid Management Pearls
- Education for Patients
- Case Study

General: Onset of irAEs



- Can be DAYS to MONTHS after administration
- Can occur AFTER treatment is discontinued
- Important to consider an irAE on patients at any time following first dose and after they have moved on to next treatment.

Acad Emerg Med. 2018 Jul; 25(7): 819–827.

General: Common vs Uncommon irAE

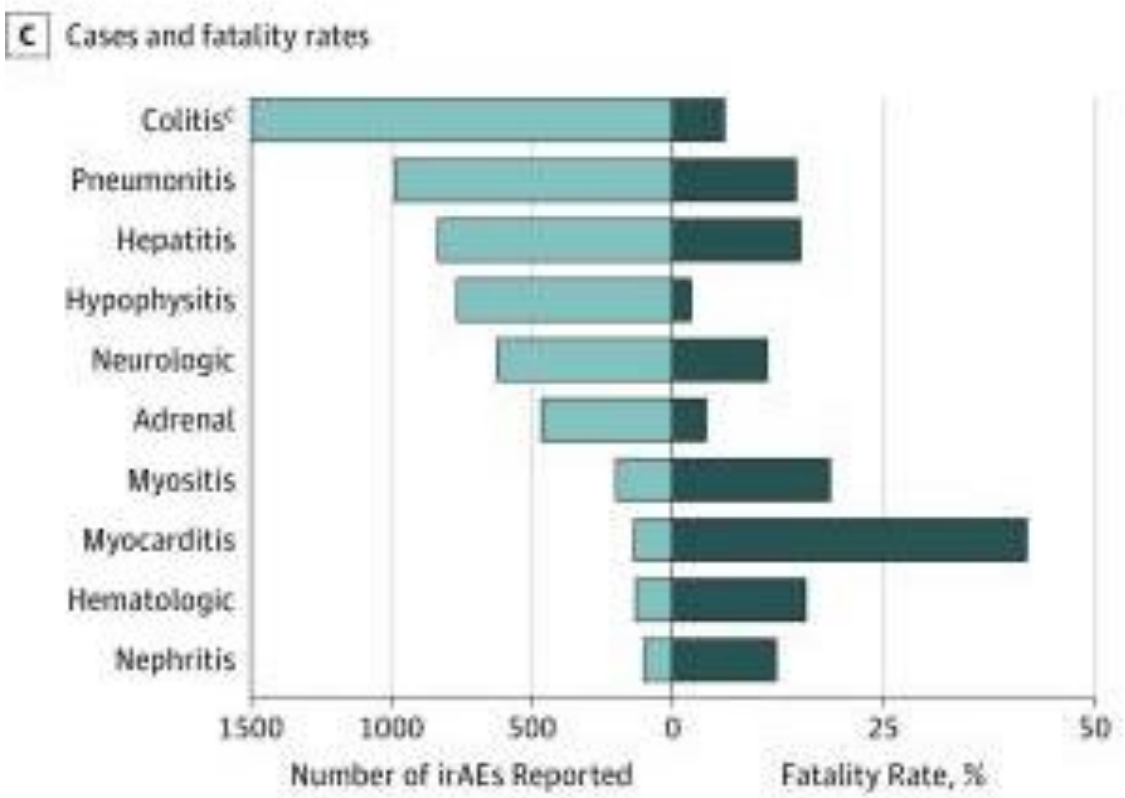
Common

- Dermatitis
- Colitis/Gastritis
- Hepatitis
- Pneumonitis/Sarcoidosis
- Thyroid dysfunction
- Sicca Syndrome

Uncommon

- Hypophysitis
- Adrenal insufficiency
- Type I Diabetes
- Myocarditis/pericarditis
- Hemolytic anemia
- Interstitial nephritis
- Uveitis
- Myasthenia Gravis/myopathy

Fatal Events with ICI



- It is the uncommon toxicity that has the potential to cause the most fatality
- Most important to consider these as possible in all cases

- Wang et al, JAMA Oncol 2018

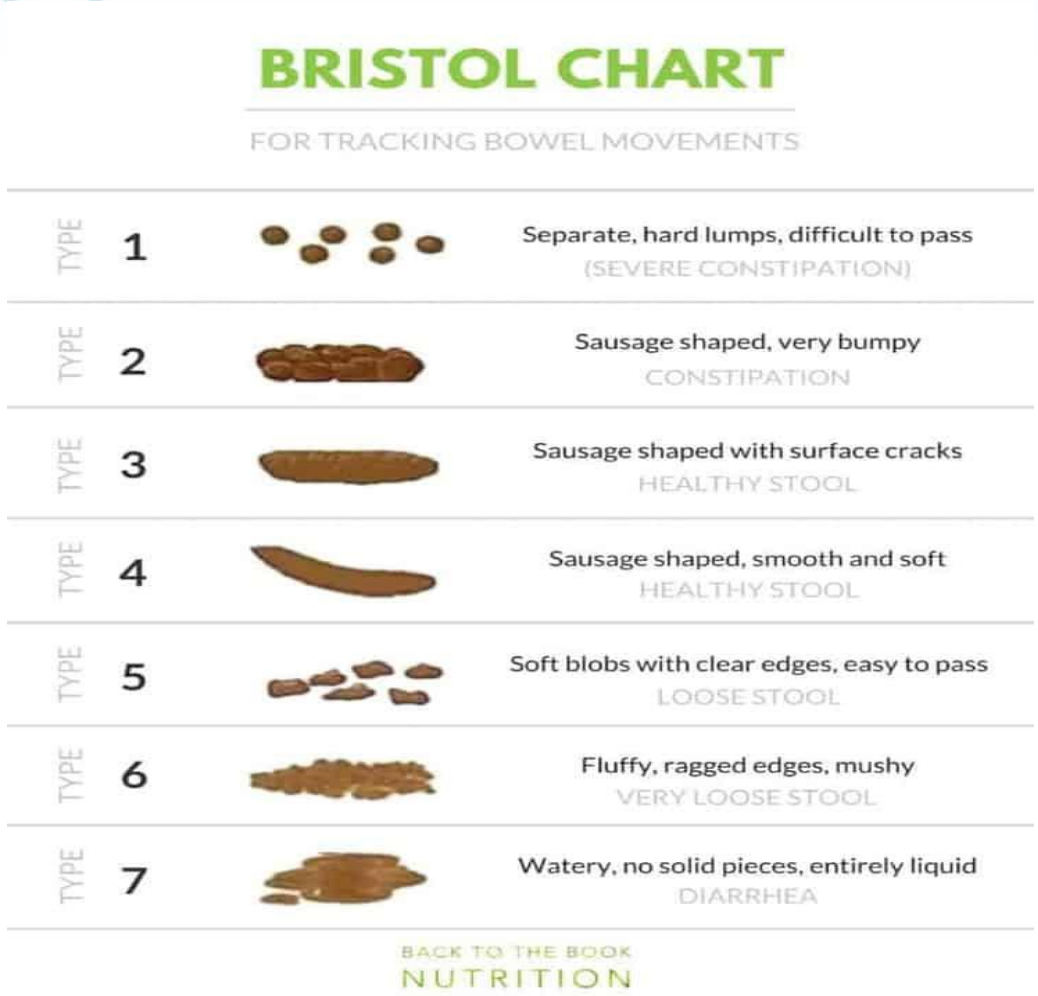
Patients with Pre-existing Autoimmune Disorders

- Ipilimumab in Melanoma Patients
  - 29% experienced a flare or pre-existing disorder
  - 29% experienced a new irAE
  - 56% experienced NO flare or additional irAE
- PD-1 in melanoma patients with a prior AE from ipilimumab OR pre-existing autoimmune disorder
  - 38% experienced flare
  - 29% experienced new irAE
  - Lower response rates in patients who remained on immunosuppressives from either the prior irAE or autoimmune disorder (15% vs 44%)

Pre-Treatment

- Take note of any underlying conditions
  - Get contact information for other physicians managing other issues
  - TEAM effort
- Establish baseline stool function/characteristic
- Bloodwork for Baseline assessment

Pre-Treatment Patient History



- Autoimmune history
- Any prior history of hepatitis or other infection
- Endocrine
- BASELINE bowel characteristic
  - Consistence
  - Frequency
  - Any associated symptoms
- Oxygen on room air

Pre-Treatment: Bloodwork

- CBC with Diff
- CMP
- TSH and Free T4
- HbA1C
- Total CK
- Infectious Disease Screen
  - Hepatitis
  - HIV antibody/antigen
  - TB testing (quantiferon gold)
- 8am cortisol and ACTH
- Baseline troponin

Follow up/Treatment visits

- Review bowel history/characteristics
- Careful history for new symptoms/signs
- Focused physical examination
- Continued labs at every visit
  - CBC, CMP, TSH, T4 free, T3 total
  - Other additional baseline labs only if issues arise

Special Consideration: Adrenal Insufficiency

- Increasing Fatigue
- Nausea/vomiting
  - Especially without other potential cause
- **Diarrhea**
- Dizziness/lightheadedness
- New exercise/activity intolerance
- Weakness
- Poor appetite
- Low blood pressure
- Weight loss
- <u>Lab findings:</u>
  - Hypoglycemia
  - Hyperkalemia
  - Hyponatremia
  - GOLD STANDARD is the cortrosyn stimulation test

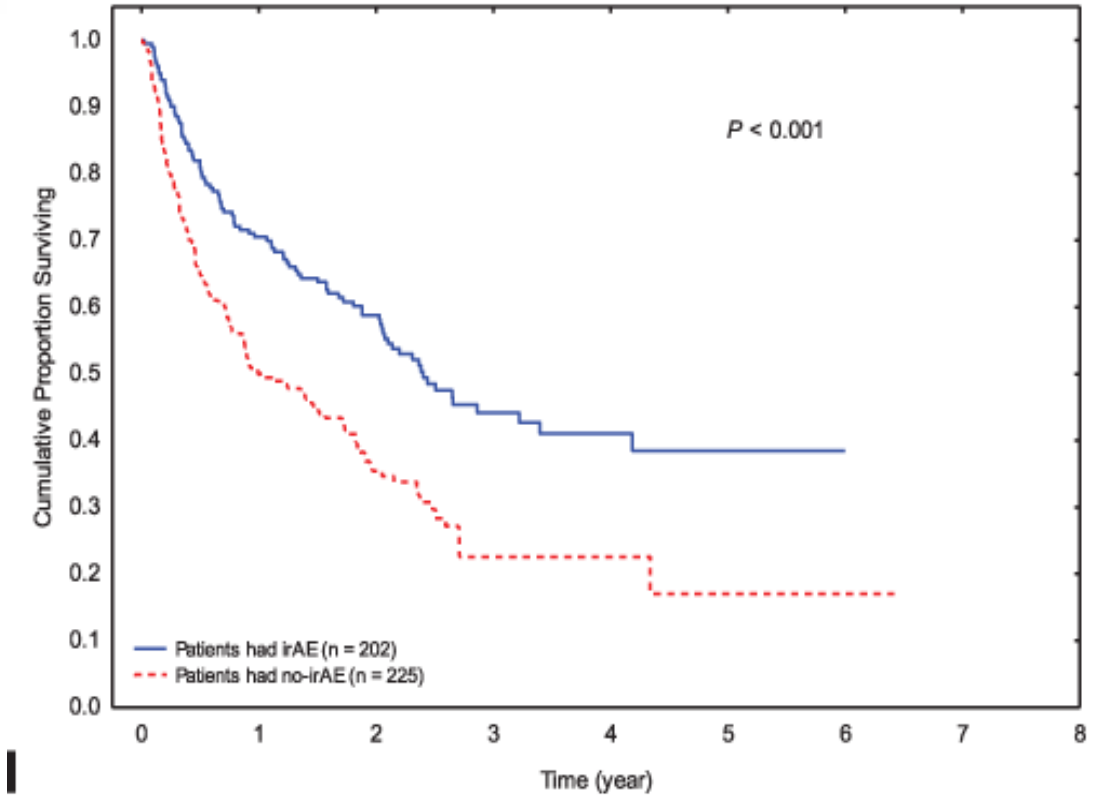
Important Patient Education

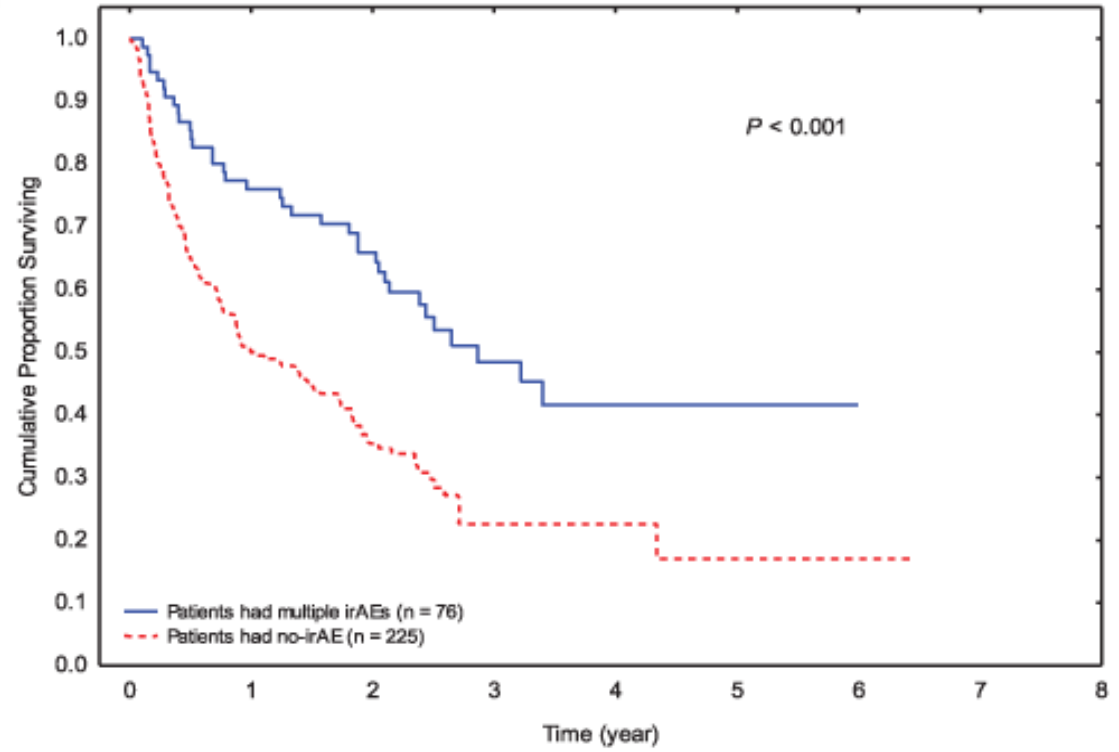
- Many immune-related events present similarly to other diseases, but the TREATMENT is sometimes very different
- Patients should ALWAYS tell healthcare professionals they are an immunotherapy patient
  - ESPECIALLY if being cared for by provider they do not know (ie: ED)
- Reassurance to patient that irAE will likely resolve over time with appropriate treatment…but may take some time to do so
  - Exception is endocrinopathy which are likely to require life-long supplementation

Steroid Management

- Introduce early for ICI toxicity
- Dose appropriately
  - 1mg/kg/day methylprednisolone or prednisone equivalent
- Taper only when irAE has resolved to grade 1
- Taper VERY slowly (over 4-6 weeks)
- Can escalate if needed during taper for recurrence of symptoms
- Use next level immunosuppression if recurrence or inability to taper

irAE and prognosis

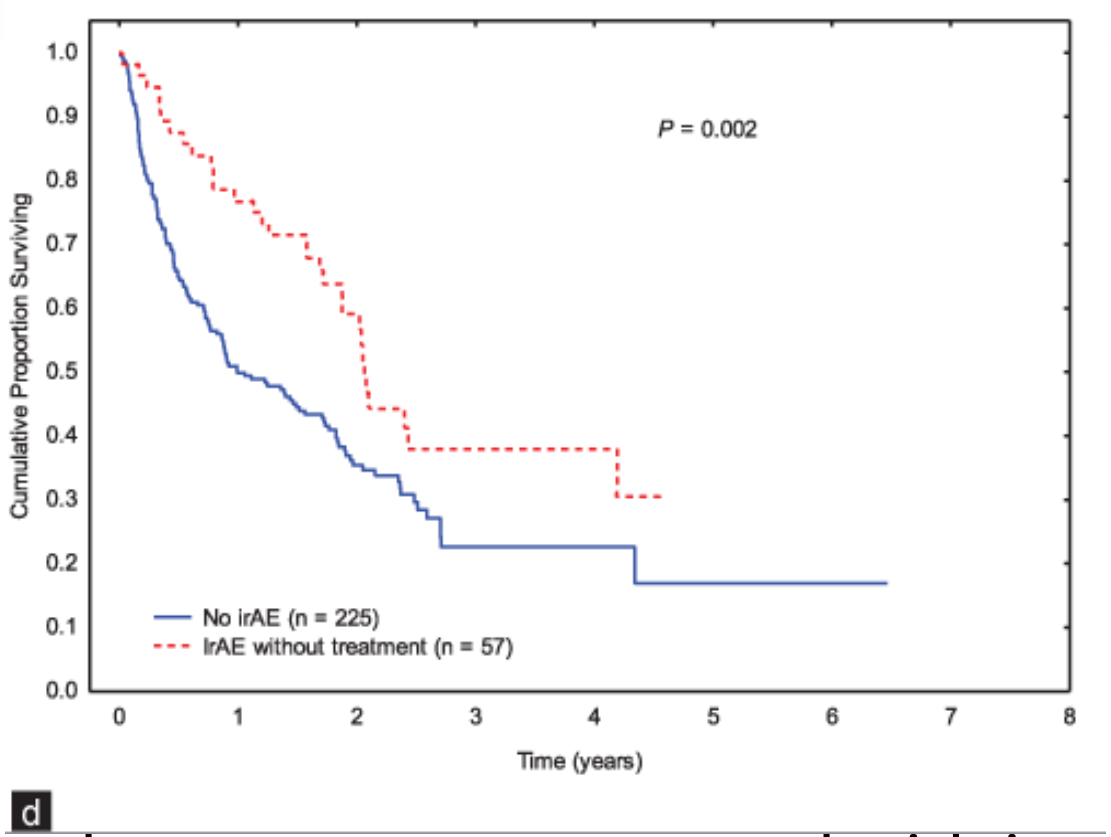




Based on **retrospective** data, patients who experience irAEs (regardless of needing treatment) may have better outcomes compared to patients who did not experience irAEs

Abu-Sbeih, J Immunother and Precision Uncol 2018

irAE and prognosis



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Immune-related adverse events not treated with immunosuppressants versus no immune-related adverse events

Abu-Sbeih, J Immunother and Precision Uncol 2018

Case Study

- AP is a 32yo female with metastatic melanoma (pulmonary, liver, and soft tissue metastases). She has received 4 cycles of ipilimumab 3mg/kg with nivolumab 1mg/kg and presents with a 4 day history of nausea/vomiting and aversion to food with diarrhea. She reports her stools are loose with 8BM/day with tenesmus, but no blood. She was also recently on a 5 day course of antibiotics from her PCP due to sinusitis.
- What is the first step in her management?

Case Study

- A: Initiate steroids at 2mg/kg/day, without further workup
- B: Give IV fluids for dehydration; loperimide, and observe
- C: Admit patient to hospital for infection work-up, colonoscopy, and IV methylprednisolone at 1-2mg/kg/day
- D: Consult GI as outpatient

Case Study

- Patient AP was admitted, GI consulted and colonoscopy, stool cultures (for ova/parasites/CMV/c.diff) were performed. CT of the Abdomen and pelvis was negative for further metastatic involvement but there was stranding around the descending colon. Cultures were negative. Colonoscopy revealed severe colitis in descending colon and ileum. Patient started on methylprednisolone 2mg/kg/day due to severity. NO improvement within 72 hours.

- What is the next step in this patient's management?

Case Study

- A: Continue current dose of steroids for a few more days
- B: Convert patient to oral steroids at 1mg/kg/day equivalent in prednisone
- C: Give infliximab or vedolizumab

Case Study

Patient AP was given infliximab at standard dosing and kept on steroids 2mg/kg/day and her diarrhea improved over the next 36 hours, with the nausea and tenesmus improving in 24 hours. Discharged home on 1mg/kg/day prednisone equivalent with a 6 week taper.

Additionally given 2 more doses of infliximab every 3 weeks during the steroid taper with no further recurrence of her diarrhea.

Would you treat this patient with further nivolumab once off steroids?

References

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